

The Canadian Council for Donation and Transplantation

# Enhancing Living Donation:

## *A Canadian Forum*

February 9-12, 2006

Vancouver, British Columbia

Report and Recommendations

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Except for:

Appendix 3:

A Report of the Amsterdam Forum on the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79(2S); S53-66. © 2005 Lippincott, Williams & Wilkins.

Appendix 4:

Barr ML, Belghiti J, Villamil FG et al. A Report of the Vancouver Forum on the Care of the Live Organ Donor: Lung, Liver, Pancreas and Intestine Data and Medical Guidelines. *Transplantation* 2006; 81(10): 1373-1386. © 2006 Lippincott, Williams & Wilkins.

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October 2006

ISBN 0-9738718-8-1

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Production of this advice/report has been made possible through a financial contribution from Health Canada.

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## Preface

The Canadian Council for Donation and Transplantation (CCDT) was established in October 2001 to improve organ and tissue donation and transplantation in Canada. The CCDT is an independent, not-for-profit corporation mandated to provide advice to the Federal/Provincial/Territorial Conference of Deputy Ministers of Health in support of its efforts to coordinate federal, provincial and territorial activities relating to organ donation and transplantation.

The CCDT utilizes three Standing Committees, Donation, Transplantation, and Tissue, as well as working groups that include non-Council experts. The standing committees bring forward standards, policies and best practices for ratification by Council. An ethicist supports the three committees in their identification and analysis of ethical issues.

The CCDT Transplantation Committee is developing a framework for action at local, provincial/territorial and national levels that will result in a sustained, systematic approach to organ transplantation. This framework will be based on evidence provided through a review of existing practices, policies or guidelines (national/international), as well as a review of science and published experience and expert consensus.

Transplantation Committee initiatives relate to various components of organ transplantation such as a) the optimal referral of potential transplant recipients, b) the assessment and listing of patients waiting for transplantation using common and transparent criteria, c) optimal organ utilization and allocation, d) the opportunities and challenges of live organ donation and e) the monitoring of transplant recipients and transplant outcomes.

The CCDT has hosted five forums to consult with health professionals and other stakeholders on best practices that can inform recommendations to the Conference of Deputy Ministers of Health (a list of these forums can be found in Appendix 8). This sixth forum, *Enhancing Living Donation*, was an exciting opportunity to bring together stakeholders in living donation to develop recommendations related to this area. A variety of factors (such as the increase in organ wait-lists and the “plateauing” of the number of both deceased and living donors) means a significant number of people are dying while waiting for an organ. We hope that initiatives such as this forum will make a vital contribution to finding new ways to help potential organ recipients.



Dr. David Hollomby  
Chair, CCDT Transplantation Committee

## Foreword

The CCDT recognizes living donation as an important area of interest. This forum was planned in the context of current and emerging developments. Included among these is the increased activity in living donor programs, as well as the need to place recommendations developed by international consensus groups into the Canadian context. There is also the recognition that, in Canada, there are issues related to significant variability in resources available to living donor programs, the donor assessment process, eligibility criteria, and provision of post-donation follow-up. There is the need to reduce the financial risk to the donor and address concerns reported by living donors.

There is no doubt that living donation presents many challenges. Medically and scientifically, there are issues such as the increasing number of individuals with additional risk factors being considered as kidney donors, the extension of living donation into liver and lung transplant programs, and the emergence of paired donor exchange programs and transplantation across immunologic barriers such as ABO-incompatibility or a positive cross-match. Other equally complex issues include the implications of anonymous or undirected living donation, and publicly solicited living donors.

In developing the agenda for this forum, we looked at the many different areas where barriers exist: risks and benefits to the donor, medical long-term follow-up, psychosocial considerations and financial disincentives.

The following points outline key assumptions, based on best evidence, that served as a starting point for discussions at the forum.

- Transplant waiting lists in Canada are growing and deceased donor organ transplants cannot meet the demand.
- Live organ donation has developed as an important alternative to deceased donor organ procurement.
- Live organ donation is accepted medical practice in Canada.
- Live organ donation is voluntary.
- Live kidney donation is cost-saving to the health care system.
- Live organ donation and transplantation must be undertaken with the highest possible standard of clinical care.
- Live organ donors do incur non-medical expenses.
- Buying, selling or any trade in organs is illegal in Canada.
- The evaluation and/or determination of eligibility of individual potential donors will continue to be the responsibility of the physicians, surgeons, and living donor programs involved with that patient.

We hope that the recommendations in this report will help to clarify and resolve issues related to living donation and ultimately have a significant impact on the health of both Canadian donors and recipients.

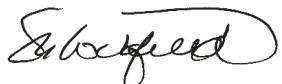
Forums of this type would have no hope of success without the work of the people who organize them. To this end, we would like to thank Tracy Brand, Dorothy Strachan and Nancy Greene. Their efforts throughout the forum process are deeply appreciated.

A special note of appreciation goes to the Steering Committee and the Forum Recommendations Group for their committed participation in the process that has led to the recommendations in this report.

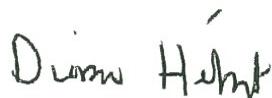
To David Hollomby, thank you for your long-standing belief in the importance of this project. To all of the participants, thank you for giving of your expertise and time to ensure the success of the forum process.

The support and guidance of the Chief Executive Officer of the CCDT, Kimberly Young, was integral to the success of the Enhancing Living Donation project.

In closing, we would like to acknowledge the support of the CCDT Council and the Chair of Council, Leah Hollins – thank you.



Sandra M. Cockfield, MD  
Forum Co-Chair



Diane Hébert, MD  
Forum Co-Chair

## Executive Summary

This forum was the sixth in a series of CCDT initiatives focused on providing stakeholders with an opportunity to explore issues and make recommendations to the Conference of Deputy Ministers of Health in the area of organ and tissue donation and transplantation.

The purpose of this forum was to build national agreement on strategies to enhance living organ donation within a safe and ethical environment, and to overcome the barriers that are current disincentives to live organ donation in Canada. Forum objectives were to:

1. Describe and confirm current and recommended practice (e.g., medical and psychosocial) for evaluating potential donors and determining eligibility for live kidney, liver and lung donation.
2. Address consent and ethical issues to support safe, well-informed choices for potential living donors.
3. Explore medical and psychosocial considerations in donor follow-up and health maintenance, and continuity of care practices in Canada.
4. Recommend options for clarifying and overcoming barriers related to reimbursement for non-medical expenses incurred by donors.
5. Clarify and discuss current life, disability and medical insurance practices affecting live organ donors.
6. Identify the implications to health care systems (e.g., financial and human resources) of increased live donation activity in Canada.
7. Identify important areas for future study and research in live organ donation.
8. Facilitate national and international networking.

The scope of the forum addressed the care of the living organ donor from the possibility of donation, through the assessment phase, and along the continuum to long-term follow-up. The following issues were not included in the scope of this forum: paired donor exchange, solicitation, buying and selling of organs, issues related to organ allocation and management of recipients of living donor organs.

Forum participants represented a multidisciplinary mix of living donation stakeholders, ensuring an inclusive approach and a range of perspectives on issues. Forum discussions focused on building consensus on key challenges and were both lively and reflective, resulting in practical and thoughtful recommendations. Extensive background documentation was provided by the Steering Committee in advance of the forum, including comprehensive literature reviews and related environmental scans. This documentation was augmented at the forum by stimulating presentations by experts from national and international jurisdictions where living organ donation is currently practiced.

To develop recommendations, participants worked in small groups guided by worksheets that provided an overview of the subject, a summary of Canadian and international practice and of existing recommendations. Following these deliberations, the Forum Recommendations Group (a multidisciplinary group representative of forum stakeholders) met to review the results of these discussions and develop consensus recommendations. These were returned to plenary for further clarification and discussion. The forum process resulted in recommendations on the following aspects of living donation:

- a. Risks and benefits of living donation related to informing the donor and to organ-specific medical/surgical risks for kidney, liver and lung transplantation.
- b. Psychosocial considerations affecting living donors.
- c. Long-term follow-up of living organ donors.
- d. Legal and ethical challenges related to consent.
- e. Economic implications of living donation related to out-of-pocket expenses and loss of income.

In addition, participants' suggestions for relevant research questions and areas for policy development were gathered and summarized.

## **Next Steps**

These recommendations will be forwarded to the CCDT Council for referral to the Conference of Deputy Ministers of Health and other stakeholders with responsibilities for implementation in the field. In addition, further discussions will be held with key stakeholder groups to support collaboration for knowledge translation and implementation.

## **Outcomes**

In the long-term, it is anticipated that this initiative will effect change in systems supporting live organ donation such that the activity can be maximized in a safe and ethical environment while enhancing confidence in live organ donation for potential and actual donors, transplant recipients and their families, members of the public and health care professionals.

A shorter term outcome of this forum was the extent of knowledge translation among stakeholders in attendance. In their forum evaluations, many participants indicated that what they had learned at the forum could be applied immediately to improve their programs and activities in living donation. In terms of success, participants rated the initiative at 4.7 on a scale of 5. As one participant wrote, "This forum was long overdue and represents a major accomplishment. There was good representation from diverse groups and the challenge questions format was excellent for eliciting valuable contributions. The organization (provision of pre-meeting documents, meeting documents, copies of presentations, etc.) and facilitation were top-rate."

Once finalized, the forum report will be distributed and made available on the CCDT web site.

## Forum Committees

<b>Sandra M. Cockfield, MD</b>	Division of Nephrology and Transplantation	Steering Committee
<b>Forum Co-Chair</b>	Immunology, University of Alberta Hospital	Planning Committee
<b>Diane Hébert, MD</b>	Division of Nephrology,	Steering Committee
<b>Forum Co-Chair</b>	Hospital for Sick Children, Toronto	Planning Committee
<b>Tracy Brand, RN, BSN</b>	Director of Initiatives, Canadian Council for Donation and Transplantation	Steering Committee Planning Committee
<b>Maureen Connelly, RN, CNephC, BScN(c)</b>	Trillium Gift of Life Network	Steering Committee Planning Committee
<b>Amit Garg, MD, PhD</b>	Division of Nephrology, London Health Sciences Centre	Steering Committee Planning Committee
<b>Scott Klarenbach, MD, PhD</b>	Division of Nephrology and Transplantation Immunology, University of Alberta Hospital	Planning Committee
<b>Dale Lien, MD</b>	Director, Lung Transplant Program, University of Alberta Hospital	Planning Committee
<b>Katrin Nakashima</b>	CCDT Transplantation Committee Member	Steering Committee Planning Committee
<b>Dorothy Strachan</b>	Strachan-Tomlinson and Associates	Planning Committee Forum Facilitation
<b>Darin Treleaven, MD</b>	Division of Nephrology, St. Joseph's Hospital	Steering Committee Planning Committee
<b>William Wall, MD</b>	Director of Multi-Organ Transplant Program, London Health Sciences Centre  Canadian Society of Transplantation	Steering Committee

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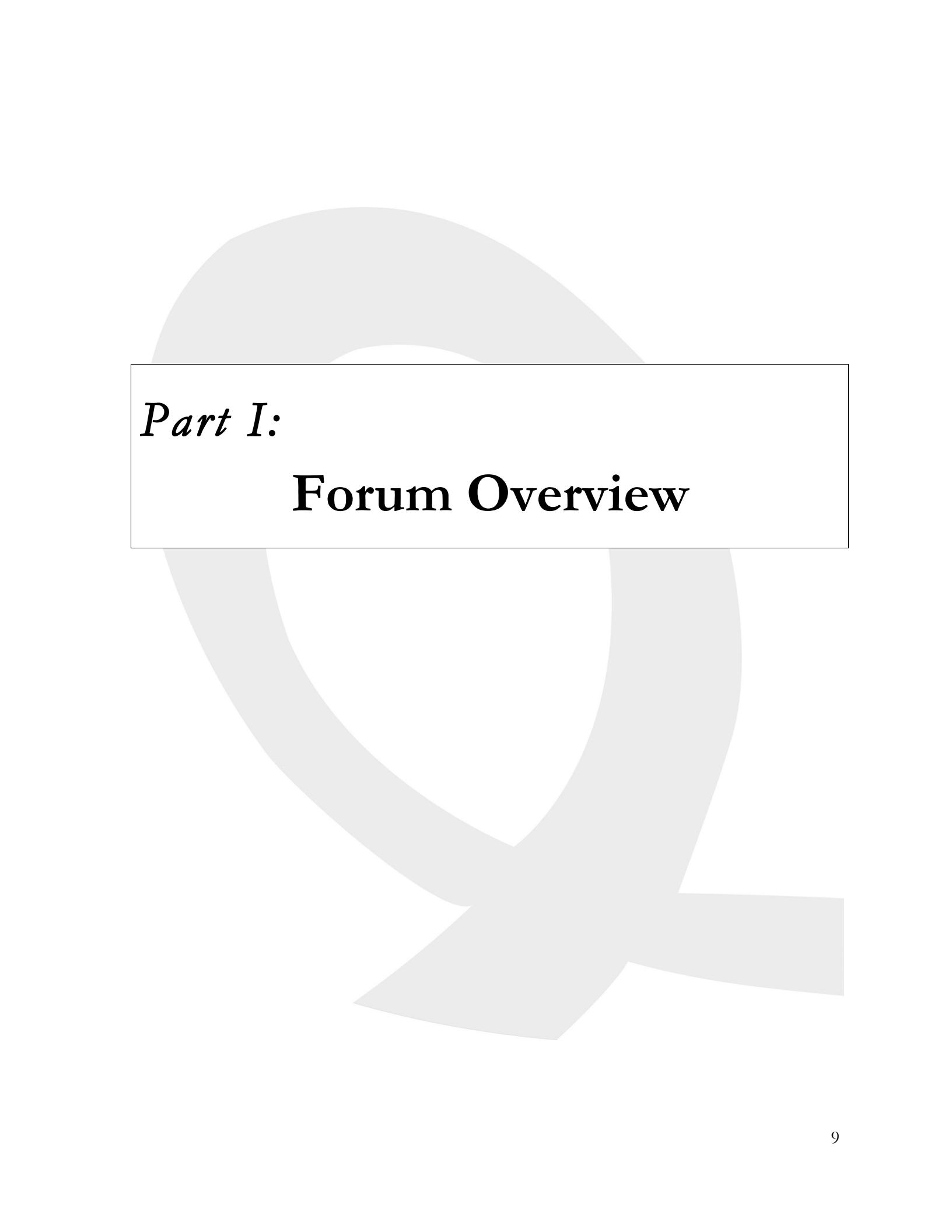
The Canadian Association of Transplantation

The Canadian Society of Transplantation

## Participating Organizations

British Columbia Ministry of Health Services  
British Columbia Transplant Society  
Canadian Association of Gastroenterology  
Canadian Association of Hepatologists  
Canadian Association of Neurology Nurses  
Canadian Association of Social Workers  
Canadian Association of Transplantation  
Canadian Association of Transplantation Nurses  
Canadian Bioethics Society  
Canadian Council for Donation and Transplantation  
Canadian Medical Association  
Canadian Society of Nephrology  
Canadian Society of Transplantation  
Capital Health Alberta  
Manitoba Transplant Program  
Multi-Organ Transplant Program – Nova Scotia  
New Brunswick Department of Health and Wellness  
Ontario Ministry of Health and Long-Term Care  
Québec-Transplant  
Saskatchewan Transplant Program  
The Law Society of Alberta  
Trillium Gift of Life Network  
United Network for Organ Sharing





*Part I:*

# Forum Overview



## **Forum Overview**

The purpose of this initiative was to build national agreement on strategies to maximize living organ donation while ensuring a safe and ethical environment for this activity, and to overcome the barriers that are current disincentives to live organ donation in Canada. This information will be forwarded to the CCDT for the purpose of developing recommendations to transplant programs and the Conference of Deputy Ministers of Health to inform current practice and relevant health policies.

## **Forum Objectives**

1. Describe and confirm current and recommended practice (e.g., medical and psychosocial) for evaluating potential donors and determining eligibility for live kidney, liver and lung donation.
2. Address consent and ethical issues to support safe, well-informed choices for potential living donors by:
  - a. identifying information on the medical, psychosocial, and economic implications of live donation, which should be shared with potential donors
  - b. recommending best practices for determining and communicating risks with potential donors.
3. Explore medical and psychosocial considerations in donor follow-up and health maintenance, and continuity of care practices in Canada.
4. Recommend options for clarifying and overcoming the following two barriers to live donation:
  - a. reimbursement for non-medical expenses incurred by donors
  - b. out-of-country billing.
5. Clarify and discuss current life, disability and medical insurance practices affecting live organ donors.
6. Identify the implications to health care systems (e.g., financial and human resources) of increased live donation activity in Canada.
7. Identify important areas for future study and research in live organ donation. For example:
  - a. expanded criteria living donors
  - b. methods for monitoring, reporting and tracking outcomes of live organ donors
  - c. identifying other barriers to live organ donation
  - d. novel strategies to increase living donor activity (e.g., anonymous living donation, paired donor exchange).
8. Facilitate national and international networking.

## Scope

The scope of the forum addressed the care of the live organ donor from the possibility of donation through the assessment phase, along the continuum to long-term follow-up.

The following issues were not included in the scope of this forum:

- a. paired donor exchange
- b. solicitation, buying and selling of organs from live donors
- c. issues related to organ allocation, and
- d. management of recipients of living donor organs.

## Key Considerations

The decision to donate an organ can be made for many reasons. The most often stated is the desire to save the life or improve the health of a relative or loved one.

Key considerations for the forum were:

1. Recommendations must be based on respect for persons, including their autonomous choices and actions.
2. The widening gap between supply and demand is putting increased pressure on the use of live organ donors without the adequate data on outcomes of live donation.
3. Unique live donor medical and psychosocial issues may mean that common criteria for eligibility may not be applicable in every circumstance.

## Process

Substantive background documents were provided by the Steering Committee in advance of the forum, including comprehensive literature reviews and related practice surveys. Each topic area was addressed during the forum using the following process:

1. Presentations by experts from jurisdictions where living donation is currently practiced were followed by open plenary discussions. Participants then worked in small groups guided by worksheets that provided:
  - a. An overview of the subject.
  - b. A summary of Canadian and international practice.
  - c. A summary of existing recommendations.
2. Small group discussions focused on specific questions related to the processes of care.  
Forum questions explored:
  - a. Informing the potential donor of the medical/surgical risks and benefits of living donation.
  - b. Psychosocial considerations affecting living donors.
  - c. Long-term follow-up of living organ donors.
  - d. The legal and ethical challenges related to consent.
  - e. Economic implications of living donation in the areas out-of-pocket expenses and loss of income.

3. Meetings of the Forum Recommendations Group (FRG) reviewed the results of small group and plenary discussions and developed consensus recommendations that were returned to plenary for further clarification and discussion.
4. Participants' suggestions for relevant research and policy development initiatives were gathered and summarized.

Forum participants represented a broad range of disciplines ensuring that discussions were inclusive and involved multiple perspectives. Forum deliberations were thoughtful, dynamic and collegial as participants focused on building agreement on key challenge questions.

Members of the FRG panel came to unanimous agreement on recommendations to inform current and future practice. Potential research and policy development areas were also identified.

## **Outcomes**

### **Immediate Outcomes**

The forum provided an opportunity for knowledge transfer among donation and transplantation stakeholders in attendance.

The CCDT will develop quality recommendations, and where appropriate implementation strategies, to be presented to the Conference of Deputy Ministers of Health concerning live organ donation practices in Canada.

### **Intermediate Outcomes**

The Live Organ Donation initiative will result in:

1. Improved practices (consistent, ethical, evidence-based) related to the evaluation, acceptance, and monitoring of live organ donors.
2. Recommendations to health authorities and government (local, provincial, federal) to inform the development of policies and identification of appropriate funding aimed at overcoming existing barriers to live organ donation.
3. Increased research opportunities in live organ donation.

### **Long-Term Outcomes**

The long-term outcomes are to effect change in the systems supporting live organ donation such that the activity can be maximized in a safe and ethical environment, while enhancing confidence in live organ donation for potential and actual donors, transplant recipients and their families, members of the public and health care professionals.

## Expert Speakers

Given the complexity of the social, medical, ethical and legal challenges related to living donation, a substantial part of the forum agenda was dedicated to presentations from family, patient and medical perspectives to enable participant learning and understanding. They are listed below in the order in which they appeared on the agenda.

### Forum Opening

Sandra M. Cockfield, MD	Challenge Address
Francis Delmonico, MD	Living Donation: Past, Present and Future

### Part I—Living Donation: Risks and Benefits

Ken Donohue, BCTS	Living Donor Experience
Linda Wright, Bioethicist	Overview: Ethical Challenges
Robert Steiner, MD	Balancing Risk and Patient Autonomy
Amit Garg, MD, PhD (kidney)	Medical/Surgical Risks of Living Donation: Organ-Specific Panel
Paul Greig, MD (liver)	
John Mullen, MD (lung)	

### Part II—Psychosocial Considerations

Sandra M. Cockfield, MD	Canadian Survey Results: Psychosocial Evaluation
Mary Amanda Dew, MD	Psychosocial Aspects of Living Donation

### Part III—Long-Term Follow-up

Sandra M. Cockfield, MD	Canadian Survey Results: Follow-up
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### Part IV—Consent: Legal and Ethical Challenges

Diane Hébert, MD	Canadian Survey Results: Consent
Tim Caulfield, Professor, Health Law	Legal and Ethical Considerations in Informed Consent
Mary Amanda Dew, MD	Donor and Family Decision Making

**Part V—Perspectives: Economic Implications of Living Donation**

Sandra M. Cockfield, MD

Canadian Survey Results: Financial Barriers

Scott Klarenbach, MD, PhD

Health Economics and Models for Reimbursement

Robert Yang, MD

Insurance Considerations

Tim Caulfield,  
Professor, Health Law

Legal Issues

## Forum Recommendations Group Members

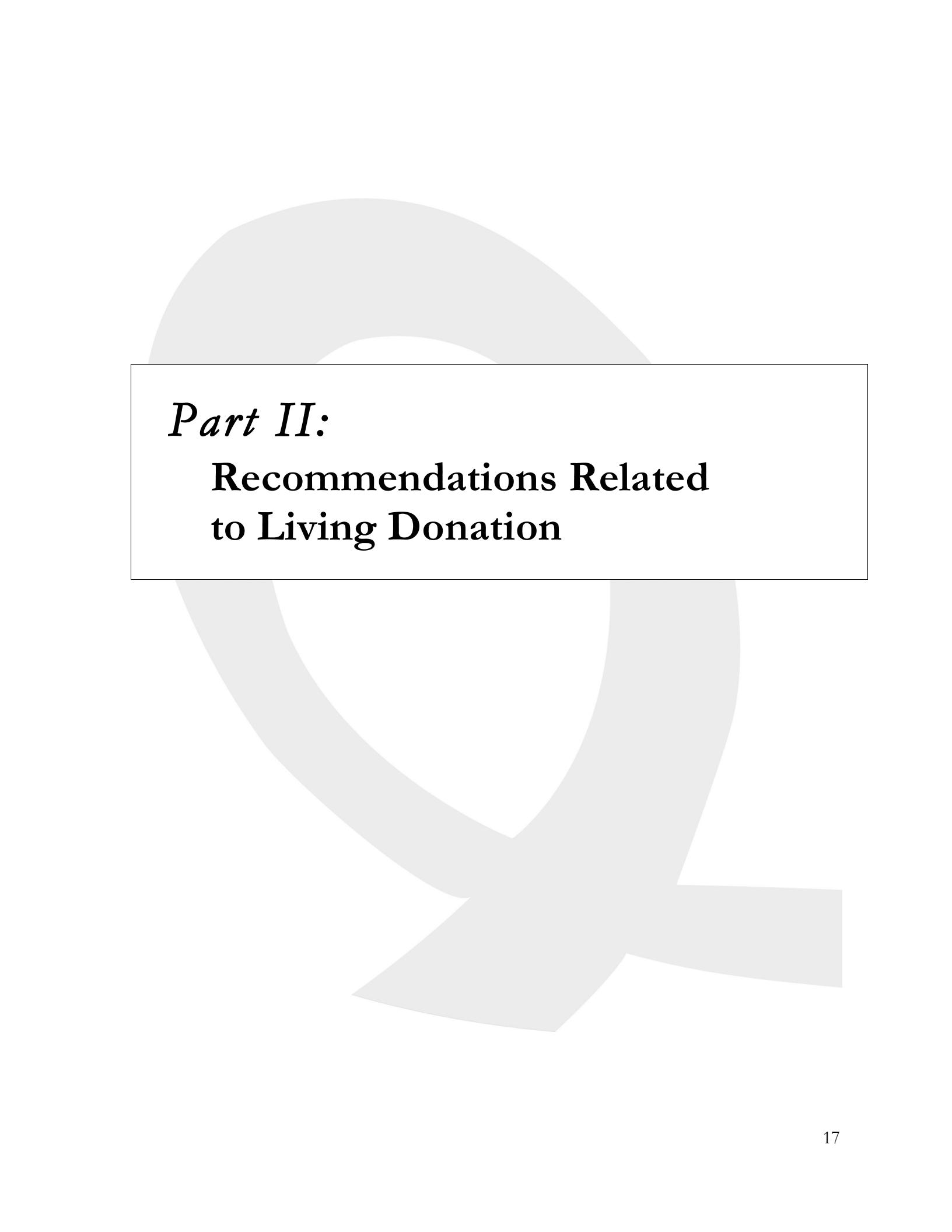
<b>Timothy Caulfield</b>	Professor, Health Law Institute, University of Alberta
<b>Sandra M. Cockfield, MD</b> <b>Forum Co-Chair</b>	Division of Nephrology and Transplantation Immunology, University of Alberta Hospital
<b>Maureen Connelly, RN, CNephC, BScN(c)</b>	Living Donation Advisor, Trillium Gift of Life Network Living Donation Coordinator, St. Michael's Hospital, Toronto
<b>Ken Donohue</b>	British Columbia Transplant Society
<b>John Dossetor, MD</b>	Bioethicist
<b>Amit Garg, MD, PhD</b>	Kidney Clinical Research Unit, London Health Sciences Centre
<b>Diane Hébert, MD</b> <b>Forum Co-Chair</b>	Division of Nephrology, Hospital for Sick Children, Toronto
<b>Mary Lou Karley, MSW, RSW</b>	School of Social Work, King's University College, University of Western Ontario, London
<b>Scott Klarenbach, MD, PhD</b>	Division of Nephrology and Transplantation Immunology, University of Alberta Hospital
<b>David Norman Landsberg, MD</b>	Director, Renal Transplantation, St. Paul's Hospital, Vancouver
<b>Dale Lien, MD</b>	Director, Lung Transplant Program, University of Alberta Hospital
<b>Vivian McAlister, MD</b>	Professor, Faculty of Medicine, Department of Surgery, London Health Sciences Centre
<b>Jean Tchervenkov, MD</b>	Director of Liver Transplantation, Royal Victoria Hospital, McGill University Health Centre, Montréal

### Advisory to the Forum Recommendations Group

<b>Tracy Brand, RN, BSN</b>	Director of Initiatives, Canadian Council for Donation and Transplantation  Forum Project Manager, Enhancing Living Donation
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### Research and Policy Development Group

<b>Isabelle Houde, MD</b>	Centre hospitalier universitaire de Quebec
<b>Darin Treleaven, MD</b>	Division of Nephrology, St. Joseph's Hospital, Hamilton



*Part II:*

## **Recommendations Related to Living Donation**



# Recommendations

Based on forum discussions, the Forum Recommendations Group made the following recommendations:

## 1. Risks and Benefits: Informing the Donor

### 1.1 Evaluation

We recommend that individuals consent to be evaluated as living donors before the assessment process proceeds beyond the initial stages of ABO blood grouping and the preliminary interview. For the purposes of this recommendation, consent<sup>1</sup> consists of providing the information and confirming that it is comprehended by the potential donor.

### Evidence

Recommendation 1.1: page 54.

### 1.2 Elements of Disclosure

We recommend that the following elements of disclosure<sup>2</sup> be included in the informed consent process:

- a. Description of the assessment process, the surgical procedure, and the recuperative period.
- b. Process for handling unexpected findings (e.g., maternity/paternity, reporting of communicable diseases).
- c. Alternative donation procedures, even if only available at other transplant centres (e.g., in the case of kidney transplantation, laparoscopic vs. open nephrectomy).

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<sup>1</sup> For more information on principles of consent, see Caulfield, Timothy. *Living Organ Donation: Consent Challenges*. Edmonton: The Canadian Council for Donation and Transplantation.

<sup>2</sup> In creating this recommendation Forum participants reviewed and adapted the practice guideline of The Consensus Statement on the Live Organ Donor (Table 1, JAMA 2000).

## 1.2 Elements of Disclosure (cont'd)

- d. Potential complications for the donor:
  - i. Surgical, including risk of death
  - ii. Long-term, including physical, psychosocial and financial
  - iii. Impact of donation on the life-style, employment, and insurability of the donor
  - iv. Impact of the discovery of an underlying condition on the ability of the individual to obtain health and life insurance.
- e. Resources available to the donor and any expenses to be borne by the donors (including potential hidden costs).
- f. Anticipated short- and long-term follow-up care.
- g. Outcomes for donors and recipients: transplant centre-specific and national.
- h. Information regarding material risks and benefits to potential recipients.
- i. Alternative treatments available to the recipient (other than living donor transplant).
- j. The potential impact of isolated abnormalities (e.g., donor hypertension) identified during the donor assessment on donor and recipient outcomes.
- k. In cases where incremental risk to either the donor or recipient is present, the information should be conveyed to both, subject to consent and a case by case balancing of rights to confidentiality.
- l. Information on possible unanticipated outcomes (e.g., non-use of the organ in the intended recipient or transmission of disease).
- m. Description of the withdrawal process, emphasizing the ability of the donor to withdraw at any time.
- n. Policies related to confidentiality of donor information (e.g., HLA typing, reason for withdrawal).

## Evidence

Recommendation 1.2: page 54.

### 1.3 Appropriate Information

We recommend that living donors receive appropriate written information in plain language concerning living donation. Options include:

- a. Web-based resources
- b. Brochures and pamphlets
- c. Itemized consent form.

Patients may also benefit from information presented in other forms. Options include:

- a. Audiocassettes, compact discs
- b. Videos, DVDs
- c. Other forms of media.

This information should be provided early in the process; however, use of these media is not meant to replace meaningful interpersonal contact.

### Evidence

Recommendation 1.3: page 54.

### 1.4 Standardized Information

We recommend that standardized organ-specific information be developed concerning the material facts, risks and benefits of living donation in the Canadian context. These tools would be developed for use by living donor programs and would be sensitive to local programs, accommodating language, faith, ethno-cultural and aboriginal concerns.

### Key Considerations

- Consent is an ongoing process that must be transparent and withstand public scrutiny.
- The provision of information is iterative and should continue throughout the process.
- Information should be:
  - evidence-based and consistent across jurisdictions
  - relevant to the context of, and comprehensible to, the patient
  - updated regularly
  - customized to the Canadian context.

- Communication should:
  - be appropriate to the target audience (e.g., verbal, written and visual)
  - take into account best practices for communicating risk-benefit and eliciting preferences.
- The consent process should not be impeded by distance (e.g., it does not need to be face-to-face).
- The consent process should be conducted in an atmosphere conducive to the meaningful exercise of options, including possible withdrawal.
- There is a need for a minimum<sup>3</sup> standard of information to be provided throughout the consent process.
- The consent process must comply with provincial law and regulations.
- Privacy and confidentiality of both the donor and recipient must be respected.
- The consent process should convey relevant uncertainties of live organ donation and transplantation.
- Tools should be developed in accordance with national standards (to be developed/maintained by an organization such as the CCDT and other stakeholders, including continuous oversight).

## Evidence

Recommendation 1.4: page 54.

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<sup>3</sup> “Minimum” should not necessarily be understood as “minimal.” “Minimal” refers to the least possible that can be done and is an absolute value. “Minimum” refers to the lowest acceptable standard, which is a relative standard, often pitched above the minimal.

## 2a. Organ-Specific Assessment: Kidney

Forum participants had the opportunity to review the published guidelines of the Amsterdam Forum<sup>4</sup> on the Care of the Live Kidney Donor. These guidelines recommended routine testing for potential living kidney donors and discussed areas of controversy in donor assessment and eligibility. These guidelines were endorsed by forum participants.

### 2.1 Overarching Recommendations

We recommend acceptance of the following two overarching recommendations of the Amsterdam Forum on the Care of the Live Kidney Donor:

- a. Prior to donation, the live kidney donor must receive a complete medical and psychosocial evaluation, receive appropriate informed consent, and be capable of understanding the information presented in that process to make a voluntary decision. All donors should have standard tests performed to assure donor safety.
- b. The current available data suggest no restriction of live kidney donation based upon the absence of an HLA match. An unrelated donor transplant is equally successful to the outcome achieved by a genetically related family member such as a parent, child, or sibling who is not HLA identical to the recipient.

### Evidence

Recommendation 2.1: page 55.

### 2.2 Use of Existing Guidelines

We recommend that in the absence of higher quality evidence, it is reasonable to refer to existing guidelines regarding the assessment and eligibility of potential living kidney donors (e.g., Amsterdam Forum). However, we recommend that these guidelines not be used as absolute criteria where risk is poorly quantified or uncertain.

### Evidence

Recommendation 2.2: page 55; see Appendix 3 for the report on the Amsterdam Forum.

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<sup>4</sup> Lippincott, Williams and Wilkins. A Report of the Amsterdam Forum on the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79: S53-S66 (included in this report as Appendix 3).

## **2b. Organ-Specific Assessment: Liver**

Forum participants had the opportunity to review excerpts from the unpublished report of the Vancouver Forum on the Care of the Live Organ Donor. This document outlines standards of care for living liver donors, including recommendations on donor assessment, morbidity and mortality and donor follow-up. The report has since been published.<sup>5</sup>

### **2.3 Minimum Investigations**

We recommend that minimum investigations for adequate medical and surgical work-up for living liver donors include:

- a. complete history and physical examination
- b. standard blood work
- c. serology
- d. imaging for liver volume, vascular anatomy and biliary anatomy (e.g., Doppler ultrasound, CT scan, MRCP)
- e. age-appropriate screening for cancer.

### **Evidence**

Recommendation 2.3: page 58.

### **2.4 Upper Age Limit**

We recommend that the upper age limit for living liver donation be 60 years.

### **Evidence**

Recommendation 2.4: page 58.

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<sup>5</sup> Barr ML, Belghiti J, Villamil FG et al. A Report of the Vancouver Forum on the Care of the Live Organ Donor: Lung, Liver, Pancreas and Intestine Data and Medical Guidelines. *Transplantation* 2006; 81(10): 1373-1386 (included in this report as Appendix 4).

## 2.5 Liver Biopsy

We recommend that not all potential living liver donors undergo a liver biopsy as part of the donor evaluation. The indications for a liver biopsy are:

- a. fatty liver on ultrasound and any other modality
- b. coarseness on ultrasound or CT scan
- c. abnormal liver enzyme.

### Evidence

Recommendation 2.5: page 58.

## 2.6 Degree of Steatosis

We recommend that a 10-20% degree of steatosis (fatty infiltration) preclude eligibility for living liver donation.

### Key Considerations

- The degree of steatosis precluding eligibility could be less for smaller livers and larger resections.
- There should be a visual assessment at the time of surgery and a second biopsy if needed.
- Steatohepatitis (excessive fatty infiltration associated with inflammation) is an absolute contraindication.

### Evidence

Recommendation 2.6: page 58.

## 2.7 Co-morbid Conditions

We recommend that the following co-morbid conditions should be considered contraindications to liver donation:

Absolute contraindications

- a. Coronary artery disease (assessed and deemed significant by an independent specialist)
- b. History of deep vein thrombosis
- c. Hepatitis C, active hepatitis B, HIV, current substance abuse, history of certain cancers (e.g., melanoma and other transmissible diseases).

Relative contraindications

- d. Diabetes
- e. Body Mass Index > 30
- f. Hypertension
- g. Smoking
- h. Hormonal therapy.

## Evidence

Recommendation 2.7: page 58.

## 2.8 Disclosure of Morbidity and Mortality Risks

We recommend that the risks of morbidity and mortality identified at the Vancouver Forum be disclosed to the donor.

Participants of the Enhancing Living Donation Forum felt that the true mortality rate is unknown, and recommended using a more conservative estimate of 1.0% for right lobe liver donors and 0.2% for left lobe liver donors.

## Evidence

Recommendation 2.8: page 58; see Appendix 4 for the report on the Vancouver Forum.

## **2.9 Recipient Not Meeting Criteria for Transplantation from a Deceased Donor**

We recommend that a potential living liver donor not be accepted for a recipient who does not meet established criteria for liver transplantation from a deceased donor.

### **Evidence**

Recommendation 2.9: page 58.

## **2.10 Fulminant Hepatic Failure**

We recommend that living donor liver transplantation may be offered in the setting of fulminant hepatic failure in certain situations where the prospect of identifying a deceased donor is low (e.g., in a pediatric patient). We recommend that, aside from expediting the routine evaluation, the assessment process should not differ from the standard protocol.

### **Key Consideration**

- Right lobe donation is necessary for larger individuals and this increases the risk to the donor. Deceased donor transplantation is preferred for larger individuals with fulminant hepatic failure and they are prioritized on the deceased donor waiting list. Transplantation with a whole liver is preferred over a partial liver in this setting.

### **Evidence**

Recommendation 2.10: page 58.

## 2c. Organ-Specific Assessment: Lung

Forum participants had the opportunity to review excerpts from the unpublished report of the Vancouver Forum on the Care of the Live Organ Donor. This document outlines standards of care for living lung donors, including recommendations on donor assessment, morbidity and mortality and donor follow-up. The report has since been published.<sup>6</sup>

### 2.11 Option of Living Lung Donor Transplantation

We recommend that the option of living lung donor transplantation be included in discussions with all potential lung transplant recipients. Because this procedure is not widely available in Canada, it should be restricted to centres with sufficient volume to support the necessary skill set and experience.

We recommend that recipients who meet the following conditions should have living lung donor transplantation as an option when:

- a. deceased donation is not available in sufficient time, and
- b. two suitable donors can be identified to provide adequate lung tissue.

We recommend that where there is a low probability of success, living lung transplantation not be offered.

### Evidence

Recommendation 2.11: page 60.

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<sup>6</sup> Barr ML, Belghiti J, Villamil FG et al. A Report of the Vancouver Forum on the Care of the Live Organ Donor: Lung, Liver, Pancreas and Intestine Data and Medical Guidelines. *Transplantation* 2006; 81(10): 1373-1386 (included as Appendix 4 of this report).

## 2.12 Minimum Investigations for Medical and Surgical Work-up

We recommend that the following minimum investigations constitute an adequate medical and surgical work-up for living lung donors:

- a. complete history and physical
- b. pulmonary function test
- c. arterial blood gas
- d. appropriate imaging to evaluate lung volumes, lung parenchyma, vascular and bronchial anatomy (e.g., chest X-ray, ventilation-perfusion scan, CT chest)
- e. evaluation of right and left ventricular function and pulmonary arterial pressures (e.g., echocardiography)
- f. routine blood work and serology, and
- g. consultations with psychiatrist/psychologist, social worker, surgeon and independent respirologist of the intended recipient's care team.

### Evidence

Recommendation 2.12: page 60.

## 2.13 Co-morbidities

We recommend that the co-morbidities identified at the Vancouver Forum should contraindicate living donation, with the exception that age 60 may be too restrictive.

### Evidence

Recommendation 2.13: page 60; see Appendix 4 for the report on the Vancouver Forum.

## **2.14 Cigarette Smoking**

We recommend that current cigarette smoking preclude donation because the long-term risks to the donor are unknown (e.g., earlier risk of COPD).

### **Evidence**

Recommendation 2.14: page 55.

## **2.15 Disclosure of Risks of Morbidity and Mortality**

We recommend that the risks of morbidity and mortality identified at the Vancouver Forum be disclosed to the donor. Individual institutional experience should also be disclosed.

### **Evidence**

Recommendation 2.15: page 55; see Appendix 4 for the report on the Vancouver Forum.

### 3. Pyschosocial Assessment

#### Overview

Various guidelines<sup>7</sup> state that a potential living organ donor should undergo a psychosocial evaluation to rule out inappropriate donors. The purpose is to:

- Evaluate the psychological, emotional and social stability of the donor.
- Identify potential factors or issues for possible intervention.
- Establish competency for informed consent.
- Evaluate the degree to which the decision is made freely without undue pressure or coercion.

#### 3.1 Psychosocial Evaluation

We recommend that the pre-donation psychosocial evaluation be conducted by a clinical social worker (with the appropriate knowledge and skill set) who is independent of the intended recipient's care team.

We recommend that a psychosocial evaluation be based on a semi-structured tool. This tool should guide discussion while enabling the latitude necessary for individual variation.

We recommend that the timing of the psychosocial evaluation be left to the discretion of the living donor coordinator on the basis of the initial interview.

#### Key Considerations

- This recommendation does not preclude involvement of a psychiatrist or psychologist. Referral is advised on identification of incremental psychological risk.
- Contact should be face-to-face wherever possible.
- The process cannot be too onerous for the donor.

#### Evidence

Recommendation 3.1: page 62.

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<sup>7</sup> Living Organ Donor Consensus Group. Consensus Statement on the Live Organ Donor. *JAMA* 284(22).

Lippincott, Williams and Wilkins. A Report of the Amsterdam Forum on the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79: S53-S66.

Barr ML, Belghitti J, Villamil FG et al. A Report on the Vancouver Forum on the Care of the Live Organ Donor: Lung, Liver, Pancreas and Intestine Data and Medical Guidelines. *Transplantation* 2006; 81(10): 1373-1386.

## 4. Donor Eligibility

### 4.1 Determination of Eligibility

Presuming donor consent has been provided, we recommend that eligibility be determined by a multidisciplinary review team. The minimum composition of this team is: a donor physician, donor surgeon, donor coordinator, and clinical social worker.

In cases where the donor is at greater risk (medical, psychosocial, financial), we recommend a multidisciplinary review team with broader representation (e.g., ethicist, psychiatrist/psychologist, independent medical or surgical specialists, patient advocate).

### Key Considerations

- Individuals who have been declined have the right to a second opinion.
- Donor autonomy does not overrule medical judgment and decision making.<sup>8</sup>

### Evidence

Recommendation 4.1: page 64.

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<sup>8</sup> The Ethics Statement of the Vancouver Forum on the Live Lung, Liver, Pancreas and Intestine Donor. *Transplantation* 2006 18(10).

## 5. Informed Consent<sup>9</sup> for Living Organ Donors

### 5.1 Independent Donor Advocates

We recommend that an independent donor advocate be involved in the assessment of a potential living organ donor. Advocacy is a continuous process which may be shared among several professionals.

We recommend that the minimum attribute of a donor advocate is independence from the intended recipient's care team.

In smaller programs, it may be difficult to identify health care professionals with the specialized expertise required to conduct the donor assessment who are NOT involved in some aspect of the recipient care team. In this setting, we recommend that a physician who is not associated with either the donor or recipient care teams (i.e., a general internist, an external specialist) act as an independent donor advocate.

### Evidence

Recommendation 5.1: page 64.

### 5.2 Independence of Donor Assessment Team Members

We recommend that the clinical social worker and medical specialist involved in the donor assessment process be independent of the intended recipient's care team. It is preferable that the living donor coordinator also be independent of the intended recipient's care team.

### Evidence

Recommendation 5.2: page 64.

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<sup>9</sup> In Canada, legal and ethical norms require all consent to be appropriately informed. In general, this means providing patients with all the information that a reasonable person in the patient's position would want to know – including information on the nature of the treatment and all material risks. This obligation also requires that reasonable steps are taken to ensure that the patient comprehended the information provided.

### 5.3 Disclosure of Information to the Recipient

We recommend that information regarding material risks and benefits for potential donors be disclosed to and discussed with the recipient within the context of the gift relationship.<sup>10</sup> This is subject to donor consent and a case by case balancing of recipient and donor rights.

#### Key Consideration

- Further analysis of obligations of the recipient team to the recipient and to the donor needs to be undertaken.

#### Evidence

Recommendation 5.3: page 64.

### 5.4 Living Donation and Minors

We strongly recommend that live organ donation from minors (<18 yrs) not be performed. In highly exceptional circumstances where such a donor may be considered, the evaluation and informed consent process should be altered to include the following requirements:

- a. An independent donor advocate: this person cannot be associated with either the donor or recipient care teams **or** the donor/recipient family.
- b. A consultation with the local ethics program.
- c. A psychosocial evaluation: conducted by an independent psychologist/psychiatrist experienced in adolescent medicine.
- d. Legal counsel.

#### Key Considerations

- Legislation as to the age of consent for living organ donation varies from province to province.
- The 18 year age limit is consistent with international standards.
- Maturity cannot be defined by chronological age.

#### Evidence

Recommendation 5.4: page 66.

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<sup>10</sup> All gifts are exchanged within a donor/recipient relationship which varies between “intimate” for family giving to almost negligible for charitable giving. All gifts involve cost to the giver, and hopefully, engender gratitude in the recipient. Living organ donation involves the additional element of possible health risk to the gift-giver, in addition to the material or financial costs.

## 5.5 Consent Forms

During the forum, participants discussed whether a surgical consent form specific to living organ donation is required. The consensus was that this not be required when the process of consent as outlined in Part I is followed.

### Key Considerations

- The consent process must comply with provincial law and regulations.
- A key element in obtaining informed consent is the assessment and documentation of comprehension of the risks and benefits of live organ donation.

### Evidence

Recommendation 5.5: page 64.

## 6. Follow-up After Donation

### 6.1 Early Post-donation Follow-up

We recommend mandatory follow-up by a medical/surgical member between 4-12 weeks and at 12 months after donation for all donors. Depending on the scope of the procedure, additional follow-up may be required during the first post-donation year.

In the case of a donor living distant from a donor/transplant centre but residing in Canada, we recommend that the living donor/transplant program shift responsibility for follow-up to the family physician or other health care provider by conveying a follow-up plan to that provider.

#### Evidence

Recommendation 6.1: page 67.

### 6.2 Long-term Follow-up

We recommend lifelong follow-up of organ donors.

We recommend that the donor be primarily responsible for ensuring that follow-up is completed beyond the first post-donation year, with coordination, education and health promotion by the donor assessment team and care provided by the family physician or other health care provider.

#### Key Consideration

- In the absence of a family physician, the living donation program should be available to provide donor-related follow-up.

#### Evidence

Recommendation 6.2: page 67.

### 6.3 Organ Specific Recommendations for Medical/Surgical Follow-up

We recommend the following organ-specific medical/surgical follow-up:

Kidney – Blood pressure, blood sugar, serum creatinine, urinalysis

Liver – Liver function test, ultrasound

Lung – Measurements of lung function, oxygen saturation and chest X-ray at six-month intervals for the first year and yearly thereafter.

## Evidence

Recommendation 6.3: page 67.

### 6.4 Access to Appropriate Future Health Care

We recommend that potential donors with no access to appropriate future health care not be eligible for living organ donation. For the purposes of this recommendation appropriate future health care includes resources sufficient to provide early post operative care, care in the event of post-operative complications, and long-term follow-up.

## Evidence

Recommendation 6.4: page 67.

### 6.5 Psychosocial Follow-up

We recommend that follow-up regarding the psychosocial impact of living organ donation be conducted after donation for every living donor during the first post-donation year.

We recommend that either the living donor coordinator or social worker associated with the living donor program (dependent on whoever has an established relationship) should ideally conduct the psychosocial assessment post-donation.

We recommend that a semi-structured interview be used to assess the psychosocial impact of organ donation following surgery.

## Key Considerations

- Proceeding with living organ donation invokes “duty of care”<sup>11</sup> of the donor by the living donor program.
- Contact should be face-to-face wherever possible.
- The process should not be too onerous for the donor.
- The follow-up should be linked to issues identified in the pre-donation assessment process.
- Quality of life self-assessment tools may be useful in follow-up care.

## Evidence

Recommendation 6.5: page 62.

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<sup>11</sup> “Duty of care” refers to the duty that all health care providers have to protect their patients’ interests and to provide their patients with an appropriate standard of care.

## 6.6 National Donor Database

We recommend that transplant data be shared at the national level to best enhance live organ donation and transplantation. Existing data sources include the Canadian Organ Replacement Registry, provincial transplant and administrative agencies, and local transplant centres. Such a strategy should be cost effective and sustainable, privacy compliant and responsive to change, resulting in information provided to transplant centres that improves the health and health care of organ donors and recipients.

We recommend that a national longitudinal donor data base be developed to track medical outcomes of living donors. The following data is required:

- a. baseline donor information (e.g., age, gender, relationship, relevant test results)
- b. donor identifiers to permit linking data with administrative databases (e.g., provincial medical services databases, Statistics Canada, Canadian Institute for Health Information, etc.)
- c. reporting of serious peri-operative complications (e.g., death, re-operation rate, re-admissions)
- d. reporting of organ failure occurring in a living donor
- e. reporting of a donor death in the year after surgery from any cause, or subsequent deaths believed to be related to the donation process.

Consideration may be given to:

- f. Data collection up to and including one year of follow-up
- g. Annual data collection beyond one year of follow-up.

## Key Considerations

- Working with existing transplant registries and administrative databases is essential.
- Resource allocation, sustainability, and methodological, legal and ethical challenges must be addressed prior to implementation.

## Evidence

Recommendation 6.6: page 67.

## **7a. Financial Disincentives to Living Donation: Out-of-Pocket Expenses**

### **Preamble**

It is recognized that living donors experience financial consequences during the assessment phase and following donation. Categories of financial risk include out-of-pocket expenses, loss of income, and potential insurance risks.

The following overarching principles apply to the recommendations in this area:

- Reimbursement is supported on the basis that it is fair and reasonable for the donor and that it removes a potential barrier or disincentive to living organ donation.
- Reimbursement must be made in a timely manner to minimize impact on the financially disadvantaged.

### **7.1 Reimbursement**

We recommend that potential living organ donors be reimbursed for out-of-pocket expenses independent of the decision to proceed with donation. Such expenses should be reimbursed within pre-defined limits for specific expenses. Types of expenses include travel (e.g., mileage, economy airfare, car rental, and parking), accommodation and meals, incidental medical expenses not covered by health insurance, child- or elder care, domestic help and certain long distance telephone charges.

We recommend that reimbursement be equitable across jurisdictions and among donors.

### **Key Consideration**

- For cases involving significant extended complications, travel costs beyond six months may be considered.

### **Evidence**

Recommendation 7.1: page 69.

## 7.2 Mechanisms for Reimbursement

Given that:

- i. the existing methods to reimburse donors [e.g., federal Medical Expense Tax credit (T2210)] are not adequate as exemplified by financially disadvantaged or marginalized patients (e.g., timeliness of reimbursements), and that
- ii. there is a wide variation of access to and level of reimbursement across Canadian jurisdictions,

we recommend that there be direct reimbursement of allowable expenses making use of existing infrastructures (e.g., federal/provincial/territorial, non-governmental organizations, and donor programs) to administer the program, recognizing that additional funding and resources may be required.

### Evidence

Recommendation 7.2: page 69.

## 7.3 Monitoring

We recommend monitoring to ensure that reimbursement does not significantly exceed actual incurred expenses.

### Evidence

Recommendation 7.3: page 69.

## 7.4 Insurance

Given that:

- i. living donors undertake certain risks in terms of current and future insurability (e.g., with respect to loan, mortgage, disability, critical illness and life insurance), and that
- ii. currently the insurance industry has a wide range of policies, attitudes and approaches to the insurance needs of individuals who may undergo donor evaluation, donor surgery, or who have previously undergone living organ donation,

we recommend that the CCDT engage in discussions with representatives of the insurance industry to develop and advocate for fair insurance policies and practices for previous and future living organ donors.

### Evidence

Recommendation 7.4: page 69.

## 7b. Financial Disincentives to Living Donation: Loss of Income

### 7.5 Remuneration of Lost Income

We recommend reasonable and fair remuneration of lost income for living organ donors.

We recommend that access to remuneration be equitable across jurisdictions and among donors.

#### Evidence

Recommendation 7.5: page 69.

### 7.6 Income Security Programs

Given that:

- i. there are existing income security programs [e.g., Employment Insurance (EI), short-term disability] for partial income reimbursement of living donors, and that
- ii. these programs are not inclusive and may not be adequate for all living donors,

we recommend that either these programs be extended, or a new program developed, to cover the specific needs and circumstances of living donors.

We recommend that family medical leave be extended to living donors.

We recommend that private or public insurance (e.g., EI and short-term disability) not be denied to living donors.

#### Key Consideration

- Special attention must be given to people who are at greatest financial risk (e.g., low-income persons, self-employed persons).

#### Evidence

Recommendation 7.6: page 69.

## Conclusion

Forum participants came to agreement on strategies to maximize live organ donation in a safe and ethical environment in Canada, while enhancing confidence in live organ donation for potential and actual donors, transplant recipients and their families, members of the public and health care professionals.

These recommendations will inform the development of an action plan by the CCDT Transplantation Committee aimed at improving existing practice and health care systems in live organ donation.

The recommendations in this report reflect minimum standards. Individual regions or programs may adopt, adapt or consider additional standards as they apply to their health care environments.

To foster optimal care of live organ donors, human and financial resources must be sufficient to support systemic change and the infrastructure required to implement these recommendations.



*Part III:*

## **Research and Policy Development**



## **Recommendations for Research and Policy Development**

Forum participants recognized that levels of evidence supporting recommendations for living donation are based on retrospective studies and expert opinions in national and international settings.

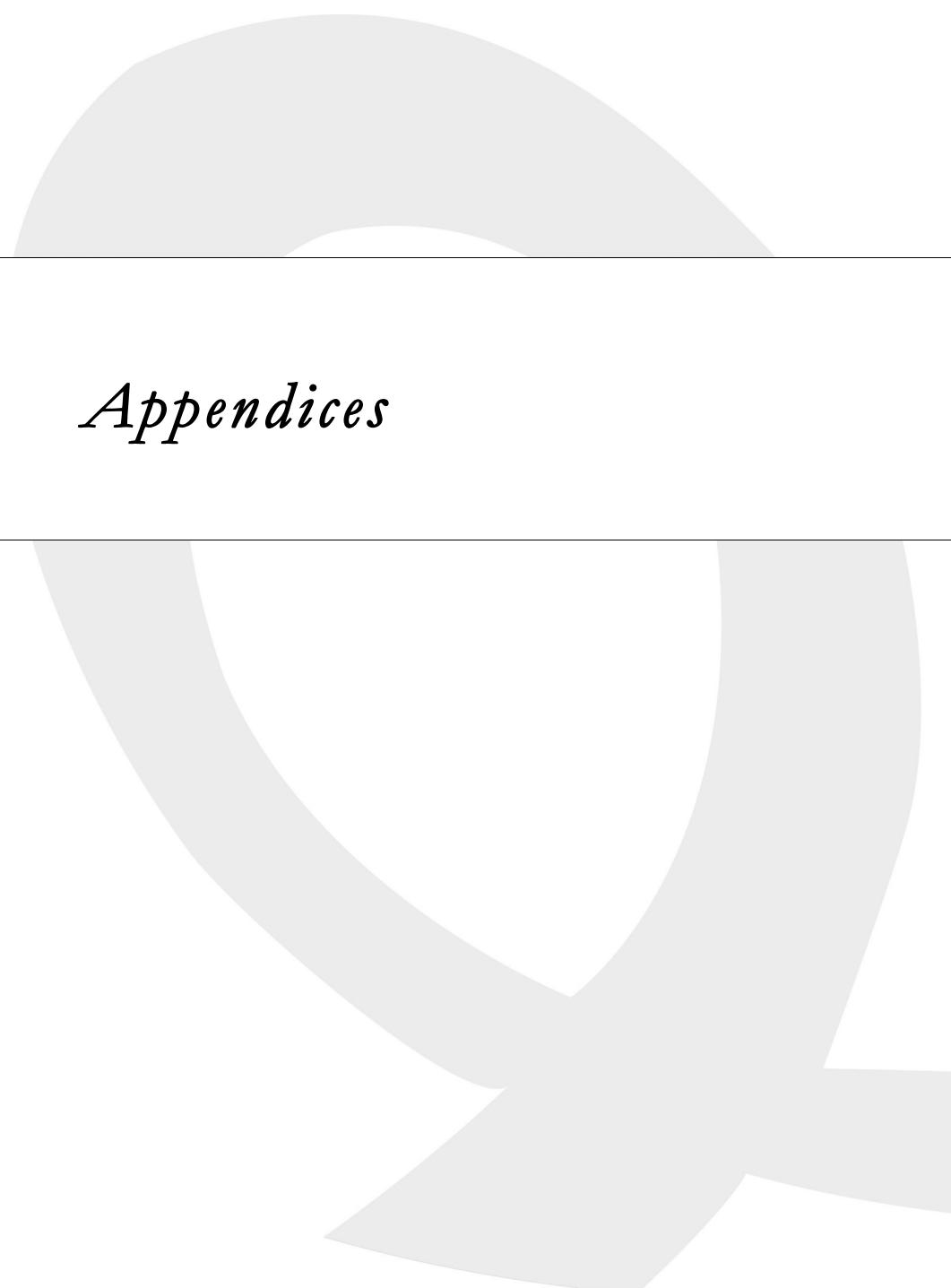
The following research topics were identified during the forum:

- Long-term medical and psychosocial risks to donors.
- Cost-effectiveness of living kidney, liver, and lung donation.
- Extent to which costs borne by the donor (e.g., out-of-pocket expenses and loss of income) affect the decision to become a donor.
- Insurability as a barrier to transplant.
- Effectiveness of strategies for communicating the risks and benefits to potential donors.
- Public attitudes towards donation, including understanding potential areas of contention.

### **Policy Topics**

- Assurance of adequate resources to support living donor programs, including additional resources for new recommendations (e.g., independent care teams and donor program follow-up responsibilities).
- Development and funding of a standard of re-imbursement for reasonable expenses incurred through all phases of donation.
- Development and maintenance of shared resource materials providing information about donation (e.g., evaluation of design of materials and resources for maintenance of materials).
- Development of a national system for the mandatory reporting of donor information; for example:
  - Baseline data (regional variation: quality assurance and fair access).
  - Early adverse outcomes.
  - Linkages to other databases.
- Other areas; for example:
  - Task force for major topic areas requiring unique expertise (e.g., exploration of the unique implications of out-of country donors and the uniform age of consent).
  - Public recognition of the living donor gift.
  - Support the development of peer-support and lobby groups.
  - Consideration of separate financial resources for severely injured donors.





## *Appendices*



# Appendix 1: Key Terms and Acronyms

## 1. Key Terms

### Clinical Practice Guidelines

In 1994, the Canadian Medical Association adopted the definition of clinical practice guidelines (CPGs) as "... systematically developed statements to help practitioner and patient decisions about appropriate health care for specific clinical circumstances." CPGs help physicians decide what is the most effective and appropriate intervention, while care maps help the health care team organize the delivery of the interventions.

Good clinical guidelines have three properties:

- First, they define practice questions and explicitly identify all their decision options and outcomes.
- Second, they explicitly identify, appraise and summarize, in ways that are most relevant to decision-makers, the best evidence about prevention, diagnosis, prognosis, therapy, harm and cost-effectiveness.
- Third, they explicitly identify the decision points at which this valid evidence needs to be integrated with individual clinical experience in deciding on a course of action.

### Donor with Incremental Risk

A donor in whom additional risk factors are identified prior to donation (e.g., a liver donor with steatosis on liver biopsy, a lung donor with a current smoking history, a kidney donor with pre-existing hypertension).

### Donor without Incremental Risk

A donor in whom no additional risk factors are identified prior to donation (e.g., renal function, urinalysis, blood glucose and blood pressure are all normal in the case of a kidney donor).

### Duty to Donor

All health care providers have a duty to protect their patients' interests and to provide their patients with an appropriate standard of care.

### Evidence-Based Medicine

Good clinical practice guidelines come from evidence-based medicine (EBM),<sup>12</sup> which is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

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<sup>12</sup> An excellent resource for EBM is the Users' Guides to the Medical Literature by the Evidence Based Medicine Working Group. The series was published in *JAMA* 1993-2000 (bibliography) and is available from Centres of Health Evidence at: <http://www.cche.net/usersguides/main.asp>.

The five steps of EBM are:

- Convert clinical information needs into answerable questions.
- Track down the best evidence with which to answer them.
- Critically appraise that evidence for its validity (approximation to the truth) and usefulness (clinical applicability).
- Apply the results of this appraisal in clinical practice.
- Evaluate the clinical performance.

EBM can address each of the five clinical objectives of:

- Achieving a diagnosis.
- Estimating a prognosis.
- Deciding on the best therapy.
- Determining harm.
- Providing care of the highest quality.

## **Gift Relationship**

All gifts are exchanged within a donor/recipient relationship which varies between “intimate” for family giving to almost “negligible” for charitable giving. All gifts involve costs to the giver and, hopefully, engender gratitude in the receiver.

Live organ donation involves the additional element of possible health risk to the gift-giver, in addition to the other material or financial costs. This emphasizes the “gift-relationship” between the two, and that there is heightened mutuality between donor and recipient. The recipient should know about this added risk element, and what it means, before accepting this type of gift. It is this element which merits this extra definition.

## **Independent Donor Advocate**

Someone who is not involved in the care of the intended recipient. This individual is charged with the responsibility of advocating for the welfare of the potential donor.

## **Informed and Comprehended Consent**

In Canada, legal and ethical norms require all consent to be appropriately informed. In general, this means providing patients with all information that a reasonable person in the patient's position would want to know, including information on the nature of the treatment and all material risks. This obligation also requires that reasonable steps be taken to ensure that the patient comprehended the information provided.

## **Local Donor**

A donor who lives in close proximity to a donor/transplant centre.

## **Performance Measures**

Performance measures are methods or instruments to estimate or monitor the extent to which the actions of a health care practitioner or provider conform to practice guidelines, medical review criteria, or standards of quality (Institute of Medicine, 1990).

## **Review Criteria**

Review criteria seek “to enable clinicians and others to assess care.” More specifically, the Institute of Medicine (IOM) suggests that they are “systematically developed statements that can be used to assess the appropriateness of specific health care decisions, services and outcomes.” To permit such assessments, the statements must usually be “suitable for retrospective medical record review of clinical practice” and capable of evaluating key pathways of past care, including guideline implementation.

Although clinicians and others may aim for excellence, review criteria frequently emphasize minimum thresholds of care. Moreover, according to Grimshaw and Russell, they should be “based on mandatory or, at worst, near mandatory elements.” Despite the IOM definition of review criteria, it is therefore important that these criteria assess appropriateness and necessity in order to show whether inappropriate and necessary care have taken place. Criteria describing appropriate care and unnecessary care are irrelevant to assessing minimum care and identifying service underuse and overuse.

## **Standards of Quality**

Standards of quality are authoritative statements of 1) minimum levels of acceptable performance or results, 2) excellent levels of performance or results, or 3) the range of acceptable performance or results (Institute of Medicine, 1990).

## 2. Abbreviations

ABO	Blood Grouping
ABPM	Ambulatory Blood Pressure Monitoring
ACOT	Advisory Committee on Organ Transplantation (US)
BCTS	British Columbia Transplant Society
BMI	Body Mass Index
BP	Blood Pressure
BSA	Body Surface Area
CCDT	Canadian Council for Donation and Transplantation
CMAJ	Canadian Medical Association Journal
CMV	Cytomegalovirus
CJA	Canadian Journal of Anesthesia
COPD	Chronic Obstructive Pulmonary Disease
CPG	Clinical Practice Guideline
CT	Computed Tomography
EBM	Evidence-Based Medicine
ECG	Electrocardiogram
EI	Employment Insurance
ELD	Enhancing Living Donation
ERCP	Endoscopic Retrograde Cholangiopancreatography
FHF	Fulminant Hepatic Failure
FRG	Forum Recommendations Group
GFR	Glomerular Filtration Rate
GP	General Practitioner
Hg	Mercury
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
ICU	Intensive Care Unit
IOM	Institute of Medicine
JAMA	Journal of the American Medical Association
LD	Living Donor
LDLT	Living Donor Liver Transplant

MRCP	Magnetic Resonance Cholangiopancreatography
NEJM	New England Journal of Medicine
PRBC	Packed Red Blood Cells
SD	Standard Deviation
UNOS	United Network for Organ Sharing

## **Appendix 2: Summaries of Evidence**

### **1. Risks and Benefits: Informing the Donor**

#### **Canadian practice:**

According to the environmental scan performed of Canadian living donor (LD) programs, preliminary information concerning risks was conveyed by telephone and/or in person by the donor coordinator by the majority of programs. Two-thirds of programs included written materials and/or references to websites.

Only two LD programs obtain consent for diagnosis, treatment and care related to the donor evaluation.

All transplant programs (n=18) indicated that they informed donors about balancing risks and benefits, effect of recipient outcomes, and risk of coercion. Freedom of choice and the impact of being declined for donation were important topics for 94% (n=17) of programs while protection of donor privacy and protection of donor interests are discussed by 15 and 16 programs respectively.

The benefits of living donation, short- and long-term medical and surgical risks, and psychosocial risks appear to be communicated by varying members of the donor assessment team. Information concerning out-of-pocket expenses (travel, accommodation, child or elder care) was reliably discussed, as was time off work. However, the impact of donation on current or future insurability was less consistently discussed (short-term coverage by 15 of 18 programs, long-term disability by 10 of 18, future insurability by 10 of 18, and future insurability due to a new health concern identified during the donor assessment by 7 of 18 programs).

#### **International practice:**

United Network for Organ Sharing (UNOS) is working to provide comprehensive information on its Transplant Living website to ensure that standardized information about the risks and benefits of organ donation is available to every potential living donor.

#### **Existing recommendations:**

The Consensus Statement on Live Organ Donation outlined the required elements of disclosure for potential living donors in Table 1 (JAMA, 2000). These have been reinforced by subsequent practice guidelines from a variety of jurisdictions.

In other areas of medicine, strategies to optimize the communication of risk include the use of visual aids, a standardized vocabulary, an understanding of cultural differences, and the use of a consistent denominator (e.g., 40 out of 1000 and 5 out of 1000 instead of 1 in 25 and 1 in 200).

## 2. Organ-Specific Assessments

### Kidney

Living donor transplants currently comprise approximately 40% of kidney transplant activity in Canada. The recipient benefits include shorter wait-times, the opportunity of pre-emptive transplantation, and superior short- and long-term outcomes. The premise for proceeding with living donation is that the “minimal” medical, psychological and financial risks of harm realized by the donor are outweighed by the definite advantages to the recipient and potential psychological benefits of altruism to the donor.

Recommended investigations for the evaluation of a living donor include a detailed medical and psychosocial history, physical examination, urinalysis, serum creatinine and assessment of glomerular filtration rate (GFR), fasting glucose and lipid profile, liver function tests and coagulation profile, chest radiograph, electrocardiogram, and imaging sufficient to evaluate the vascular anatomy.

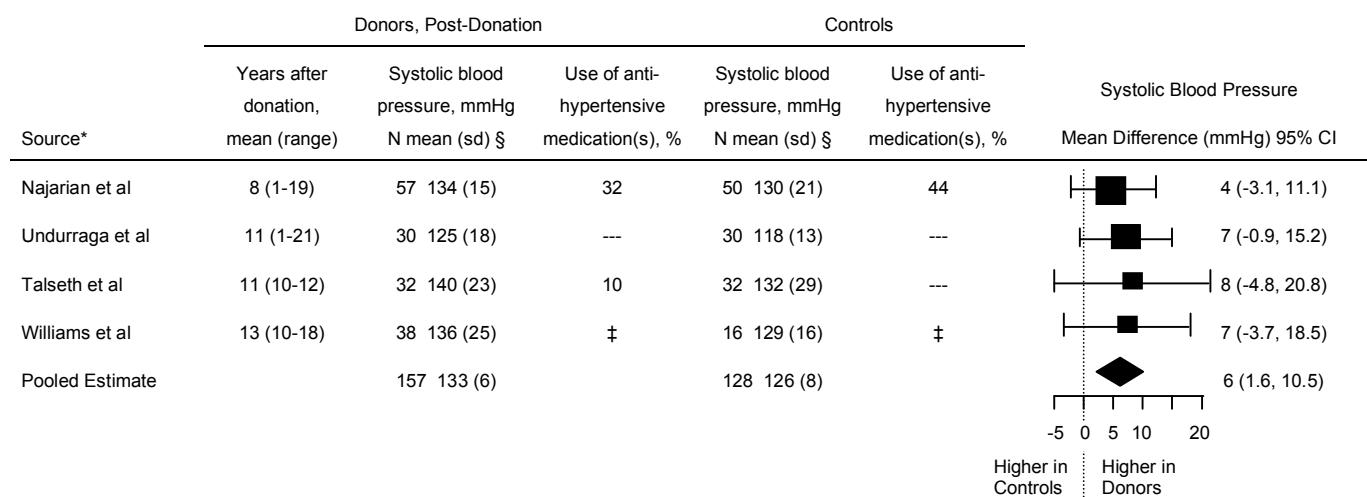
Generally accepted criteria that preclude living kidney donation include ABO-incompatibility and a positive cross-match between the donor and recipient (although certain centres are exploring strategies to overcome these barriers), significant medical conditions (e.g., diabetes, symptomatic ischemic heart disease, congestive heart failure, etc.) that substantially increase peri-operative or long-term risk, active malignancy or infection. There is substantially more debate regarding eligibility of those with well controlled hypertension, donor Body Mass index (BMI) > 35, or the presence of isolated laboratory abnormalities such as microscopic hematuria, largely due to concerns about long-term outcomes. Little is known about either the long-term risks to such donors or the long-term outcome of kidney transplants from such donors.

Short-term risks of living donation are relatively well-established. The peri-operative risk of death is less than 0.03%; the mortality rate does not appear to be influenced by the surgical approach. The risk of re-operation is < 1% for laparoscopic donor nephrectomy and <0.4% for open nephrectomy. The pulmonary embolism rate is less than 2%, and morbidity such as minor wound infections, urinary tract infections, and low-grade fever occurs in less than 10% of patients. Overall, an average hospitalization lasts less than a week and most patients feel fit enough to return to work within a month after the procedure.

Long-term risks of living kidney donation remain less well-established and studies conducted to date have important methodological limitations. It would appear that blood pressure increases by ~5 mmHg after donating a kidney above the natural increase which occurs with normal aging (see figure below). Most studies have not suggested an increased rate of hypertension following donation. Kidney function (GFR) decreases 10 mL/min after donation, and subsequent reductions in kidney function are as anticipated with normal aging. In follow-up, approximately 13% of donors developed a GFR between 30 and 59 mL/min and 0.4% a GFR less than 30 mL/min. There have been rare cases of kidney failure after kidney donation. In cases of reduced kidney function or kidney failure after kidney donation, the extent to which donating a kidney per se was a contributing factor is uncertain. A small proportion of these individuals would have developed these outcomes even if they had not donated a kidney. Kidney donation results in small increases in urine albumin excretion; 3% of donors may develop proteinuria of > 1 g/d on long-term follow-up. To date no study using appropriate controls has examined whether donating a kidney increases the risk of premature death or cardiovascular disease over

the long-term. This concern has been raised due to the observation that renal insufficiency is an independent risk factor for cardiovascular disease in the general population.

**Fig 1.1 Controlled studies of systolic blood pressure at least 5 years after kidney donation**



### Canadian practice:

The environmental scan conducted prior to this forum revealed that there is considerable uniformity between Canadian living kidney donor programs in the medical tests considered routine components of a donor evaluation, such as serum creatinine, urinalysis, creatinine clearance, and timed excretion of protein. Most programs assess fasting blood glucose and lipid profiles. However there is substantial variability in the use of other tests such as 24 hour ambulatory blood pressure monitoring, urine microalbuminuria, glucose tolerance tests, or radio-isotope assessment of GFR.

Not unexpectedly, there is considerable variability in practice particularly when it comes to accepting a potential living donor with hypertension or mildly abnormal renal function. In the case scenario involving a 50 year old male with well-controlled hypertension on a single anti-hypertensive agent, 5 of 14 centres responded that they would never accept such an individual as a kidney donor. However, other centres would rarely ( $n=2$ ), sometimes ( $n=5$ ) and usually ( $n=2$ ) accept this individual as a living kidney donor. No program accepted a potential donor with diabetes.

### **International practice:**

There is also considerable heterogeneity of practice as described in surveys of practice in the United States and France when it comes to exclusion criteria based on medical risk factors of hypertension, risk for diabetes, the presence of proteinuria or mild renal insufficiency.

For example, in the case of donor hypertension, a survey of 231 UNOS-approved transplant centres (Bia et al., Transplantation, 1995) revealed that 64% of centres excluded a donor taking an anti-hypertensive medication, while 54% would exclude those with persistent borderline hypertension. In a survey of programs in France (Gabolde et al., Nephrol Dial Transplant, 2001), 88% of programs would exclude someone with a normal blood pressure (BP) on antihypertensive therapy; 70% would exclude someone with persistently elevated BP  $\geq 130/90$  without medication; 42% would exclude someone with an occasional BP  $\geq 130/90$  without medication, and 28% would exclude someone with a BP  $\geq 130/90$  at the doctor's office despite having home readings of  $\leq 120/80$  at home.

### **Existing recommendations:**

Report of the Amsterdam Forum on Live Kidney Donation (Transplantation, 2005): This report suggests certain exclusion criteria based on the presence of donor diabetes, hypertension (BP  $> 140/90$  by ABPM in individuals  $< 50$  years of age), donor proteinuria  $> 300$  mg/day, or donor GFR  $< 80$  ml/min or 2 SD below normal (based on age, gender and BSA correction).

European Renal Association-European Dialysis and Transplant Association (Nephrol Dial Transplant 2000): Exclusion criteria include: “reduced GFR (in comparison to normal range for age), proteinuria  $> 300$  mg/day, microhematuria (except when a urologic evaluation and possible kidney biopsy are normal), or hypertension without good control”.

UK Guidelines for Living Donor Kidney Transplantation (2000): “... hypertensive end organ damage is an absolute contraindication to kidney donation. If a prospective donor is on treatment for hypertension, it may still be reasonable to consider proceeding if their blood pressure is well controlled (diastolic  $\leq 83$  mmHg).... A creatinine clearance of 80 ml/min/1.73 m<sup>2</sup> is a reasonable lower limit for kidney donation.”

## **Liver**

Living donor liver transplantation developed in response to the critical shortage of donor organs for small children and has quickly been established in major transplant centers. It has had a large impact on reducing the mortality of small children on the waiting list and it significantly reduced their waiting time. The bond between a parent and child and the desire of a parent to save the life of an infant justified the operation and its rapid acceptance, in spite of the risk for the donor.

Living liver donation between adults using the right lobe developed eight years ago as an extension of the adult-to-child experience. Greater controversy has surrounded live donor liver transplantation between adults because of the magnitude of the surgery and the greater risks for the donor, including death. The expected outcome for the recipient should justify the donor risk, and the recipient should meet the same criteria for receiving a graft from a living donor as he or she would to receive a transplant from a deceased donor.

### **Canadian practice:**

The environmental scan conducted prior to this forum revealed that there was considerable agreement between the two living liver donor programs who responded to the survey in the medical assessment of the potential living liver donor. Tests that were performed in addition to liver function tests and ABO grouping included fasting blood glucose, creatinine, CT volumetry and MRCP. In both programs, the potential donors were told about the risks of biliary complications, possible liver failure, need for reoperation and chronic pain. The reasons for not accepting donors were: size incompatibility 24%, vascular anatomy 24%, donor choice 13%, medical concerns unknown before 13%, co morbidity 13% and age 13%. In the case scenario involving a 30 year old female with a BMI of 32 being assessed for liver donation, both programs answered that they would sometimes accept such an individual for donation.

### **International practice:**

The results of a national survey in the US showed that guidelines for evaluation of donors are not standardized; most donors were assessed by a hepatologist, social worker and psychologist/psychiatrist; only half the centres used a hepatologist not associated with the transplant team or an independent ethicist; invasive procedures (biopsy, ERCP or angiography) were performed inconsistently with programs performing these procedures in none, some or all potential donors; the risk of death quoted by the transplant teams varied by more than a factor of 10, from less than 0.1% to 1%. (Brown et al., NEJM, 2003).

#### **Peri-operative Complications:**

- Cannot be definitively stated
- Catastrophic complications – 0.4 to 0.6%
- Death for left lobe donor – approximately 0.1%
- Death for right lobe donor – approaches 0.5%
- Biliary complications requiring intervention – 6%
- Estimated crude morbidity rate – 31%
- Estimated time to recovery – 3 to 4 months.

**Existing recommendations:**

There is no universally accepted protocol for donor evaluation but there is consensus that the assessment should ensure the physical and mental health of the donor, that the motives of the donor are appropriate and that the donor liver is healthy and favorable in terms of size and anatomy. The risk of death cannot be definitely stated because no registry exists that includes all donors. The rate of complications is higher in right lobe donors than in donors of the left lateral segment and the complications are more serious.

Recommendations from the recently held international Vancouver Forum on the Care of the Live Organ Donor (September 2005) have yet to be published (manuscript submitted to Transplantation). Outcome results from this forum for liver donation included the following recommendations on donor evaluation, medical suitability and responsibility and duration of follow up. The indications for live donor liver transplantation should be the same as those established for deceased donor transplantation with the exception of institutionally-approved protocol studies that consider live donor transplantation preferential to liver transplantation from a deceased donor. Live liver donation should only be performed if the risk to the donor is justified by the expectation of an acceptable outcome in the recipient. The patient and graft survival of a live donor transplant should approximate the expected outcome for a recipient with the same disease etiology undergoing a deceased donor transplant.

The Vancouver Forum further recommended that the donor evaluation be done by an independent donor advocate. Routine imaging to assess liver volume and vascular anatomy is recommended but routine donor liver biopsy remains controversial. Suggested indications for a donor biopsy include abnormal liver function tests; donors with a BMI > 30; genetically-related donors where the recipient has autoimmune hepatitis, primary sclerosing cholangitis, or primary biliary cirrhosis; steatosis or other abnormalities on imaging studies. No absolute upper age limit or high BMI were recommended to rule out donation but > 60 years and >30 BMI were discussed as increasing surgical risks. Donors should be followed up for at least one year after donation.

Fulminant hepatic failure (FHF) is an acceptable indication for emergency live donor liver transplantation. Centres performing live donor liver transplantation for FHF should have the capacity to expeditiously complete the donor evaluation and education process. The ability to perform a rapid evaluation of the potential donor including blood tests, electrocardiogram, chest x-ray, pulmonary function test, echocardiography, imaging studies of liver, psychosocial assessment and evaluation by the ethical board in a 24 to 48 time period is considered optimal.

## Lung

Living lung donation remains a relatively new procedure done only in a few centers with still-limited worldwide experience. As such, standards for donor workup and selection remain to be established and verified. Until comprehensive information on the long term outcomes for both donors and recipients becomes available, the criteria for donation will continue to be dependent on local experience and practices. The requirement for two donors for every recipient presents unique challenges and additional complexity.

The usual quoted mortality for surgical lobectomy in non-donors is < 1%. To date there has been no reported peri-operative mortality of a lung donor. There have been life-threatening complications in three donors (0.5%) with an intra-operative ventricular fibrillation arrest and two with a post-operative pulmonary artery thrombosis. The mean length of the initial hospitalization following the lung lobectomy has been 8.5 days (range 3 – 36). Approximately 4% of live lung donors have experienced an intraoperative complication that included ventricular fibrillation arrest, the necessity of a right middle lobe sacrifice 7 (1.3%), the necessity of a right middle lobe re-implantation 6 (1.1%), the necessity of a non-autologous transfusion PRBCs 5 (0.9%) and a permanent phrenic nerve injury. Approximately 5% of donors experienced complications requiring surgical or bronchoscopic intervention. These complications included bleeding, bronchopleural fistula, pleural effusion, empyema, bronchial stricture, pericarditis requiring pericardectomy, arrhythmias requiring ablation and a chylothorax.

There were 14 (2.6%) live lung donors that were readmitted to the hospital because of a pneumothorax, an arrhythmia, empyema, pericarditis, dyspnea, pleural effusion, bronchial stricture, bronchopleural fistula, pneumonia, hemoptysis or dehydration. The long-term (> one year) donor complaints of live lung donors include chronic incisional pain, dyspnea, pericarditis, and non-productive cough.

### **Canadian practice:**

The environmental scan conducted prior to this forum received responses from two programs. Both agreed that the mandatory medical workup for prospective donors should include routine blood work, arterial blood gases, pulmonary function studies, chest radiograph, augmented CT chest, ECG, echocardiogram, ventilation-perfusion lung scan with regional quantitation, thoracic dimensions, and a comprehensive personal and family history. Both also agreed on mandatory psychosocial evaluation. The composition of the evaluating teams were similar. Long-term follow-up of donors was identified as an important aspect.

### **International practice:**

In contrast to the Amsterdam Forum on the Care of the Live Kidney Donor, no such published consensus exists for living lung donation. A recent international conference was held in Vancouver in September 2005 under the guidance of the Ethics Committee of the Transplantation Society to address this issue and a publication is being prepared. However, the assessment of potential donors in other international centers appears consistent with that of the Canadian centers.

The Vancouver Forum suggested the following eligibility criteria for living lobar lung donation:

- Age 18-60 years and able to give informed consent
- No active tobacco smoking or a significant smoking history
- No active lung disease/previous ipsilateral thoracic surgery
- No identifiable risk for familial lung disease (i.e., familial forms of idiopathic lung disease or pulmonary artery hypertension)
- No cachexia ( $BMI < 18 \text{ kg/m}^2$ ) or obesity ( $BMI \geq 30 \text{ kg/m}^2$ )
- ABO blood type compatibility with recipient
- Donor lobe size compatible with recipient hemithorax
- Normal pulmonary function and arterial blood gas results
- No conditions that significantly increase the risk of general anesthesia, surgery, and postoperative recovery
- No psychosocial, ethical issues, or concerns about donor motivation
- Not pregnant
- No active malignancy
- No active significant infection (HIV, hepatitis, acute CMV).

**Existing recommendations:**

All centers appear to agree on:

1. The comprehensive evaluation on the potential live donor includes a very complete medical workup, psychosocial assessment and detailed discussion of risks and benefits before consent is obtained.
2. The ideal donor to recipient size ratio has yet to be determined.
3. Uniform criteria for donor acceptability have yet to be agreed upon and require long-term outcome data.
4. Donor follow-up is an important aspect that requires adequate attention and funding.

### **3. Psychosocial Assessment**

A psychosocial assessment of a living donor is considered an integral component of the donor evaluation. In most situations, the results of the psychosocial evaluation would not be used to exclude individuals from organ donation but rather to inform the donor team about interventions that may enhance the potential donor's well-being and minimize the chance of adverse psychosocial outcomes during the evaluation process and following surgery.

Suggested core components of this evaluation include:

- An exploration of the motivation for organ donation (how the decision was made, evidence of coercion or inducement, expectations and ambivalence)
- The nature of the relationship between donor and recipient (strengths, past conflicts/difficulties)
- Attitudes of significant others toward donation (availability of emotional and practical assistance)
- Knowledge and comprehension about the surgery and recovery
- Review of work- or school-related issues
- Mental health history and current status (psychiatric disorders, substance abuse, cognitive ability, competence, and capacity)
- Psychosocial history and current status (marital stress, living arrangements, religious beliefs and orientation, concurrent stressors, coping strategies).

The available literature suggests that the majority (>90%) of living donors do not regret their decision to donate. Post-donation distress (depression or anxiety) rates are similar to those observed in the general population. Low percentages of donors (median of 11%) feel that their relationships with their spouses or families have been negatively affected while fewer than 5% report a worse relationship with the recipient. In general, donors' perceptions of their physical, functional, psychological and social well-being are either similar to or significantly better than that reported by the general population. The major area of concern, reported by a median of 23% of donors, is financial hardship resulting from organ donation.

Limited reproducible data are available regarding factors associated with inferior post-donation psychosocial outcomes. Outcomes do not appear to be related to peri-operative course or complications, a history of pre-donation psychiatric disease, or the nature of the past relationship with the recipient. However, factors such as a more distant relationship (in the case of related donors), motivations of repairing or restoring relationships within the family, and greater ambivalence prior to donation may be important. There is little data concerning the impact on psychosocial outcomes of the type of organ donated, donor demographics, or the type of donor-recipient relationship. Interestingly, recipient outcomes of graft failure or death do not appear to influence donor psychosocial outcomes.

### **Canadian practice:**

The environmental scan conducted prior to the forum revealed that the great majority (16 of 18 living donor programs) indicated that psychosocial assessment of the potential living donor is mandatory. Two indicated that it was not mandatory in their program. Of the 16 programs that consider this component essential, a social worker is involved in 15; in the remaining program a psychiatrist is routinely consulted. In addition to the social worker, some programs also consulted either psychiatry (n=5) or psychology (n=5). The format of these assessments varied somewhat from program to program but most used a structured interview (n=6) or a combination of interview and discussion (n=10). In some programs (n=2) an additional tool in the form of a psychological assessment tool was utilized. Assessments usually take a total of 45 – 90 minutes according to responding programs.

The British Columbia Transplant Society has developed a tool for the psychosocial assessment of non-directed (or anonymous) living kidney donors. The utility of this tool, or modifications thereof, has not been reported in the more common setting of directed living donation.

### **International practice:**

In a US study, 79% of centres routinely employ a social worker as part of the donor assessment. However fewer than half (46%) include routine psychological evaluation of potential donors unless there is concern about the voluntary nature of their decision (Bia et al., *Transplantation*, 1995).

In a French survey of living donor programs, potential living donors underwent a systematic psychological assessment in 53% of programs. The social situation of potential donors was explored by a social worker in 38% of centres, while 35% of centres did not use such an assessment (Gabolde et al., *Nephrol Dial Transplant*, 2001).

### **Existing recommendations:**

There are no widely adopted standards for the content or format of the psychosocial evaluation.

Consensus Statement (JAMA, 2000): “A psychosocial evaluation is necessary for each potential donor. The psychosocial evaluation should be performed by a trained mental health professional (i.e., clinical social worker, psychologist, psychiatrist, or psychiatric nurse) experienced in transplantation. The psychosocial evaluator should be a professional not involved in the care of the recipient.”

Report of the Amsterdam Forum on Live Kidney Donation (*Transplantation*, 2005): Not stated.

European Renal Association-European Dialysis and Transplant Association (*Nephrol Dial Transplant*, 2000): “Psychosocial evaluation: optional.”

UK Guidelines for Living Donor Kidney Transplantation (2000): “the doctor caring for the donor is responsible for informing them of the potential psychosocial after-effects of kidney donation....An independent assessment of the psychosocial implications for the donor may be helpful....In many transplant centres a designated person (usually a transplant coordinator or nurse practitioner) plays a key role in organizing the medical assessment of the prospective donor... and are able to provide the support needed by the donor...”

## 4. Consent: Legal and Ethical Challenges

The Consensus Statement on Live Organ Donors (JAMA, 2000) states that “The person who gives consent to be a live organ donor should be competent, willing to donate, free from coercion, medically and psychosocially suitable, fully informed of the risks and benefits as a donor, and fully informed of the risks, and benefits, and alternative treatment available to the recipient. The benefits to both donor and recipient must outweigh the risks associated with the donation and transplantation of the living donor organ.”

In order for consent to be valid, it must be informed, voluntary and provided by an individual who has capacity. Donors must be provided with “material information” concerning the proposed procedure; “material information” is defined by what a reasonable person in that patient’s position would want to know. The potential for conflicts of interest must be acknowledged by the program and where possible, avoided or moderated. Consent must be free of coercion or undue influence by family, the recipient, friends, or health care professionals. The consent process must be structured to allow for careful reflection and ample opportunity to explore motivation and anxieties. The individual must have the cognitive ability to understand the nature and consequences of organ donation. Potential donors must retain the right to withdraw consent; the reason for withdrawal must remain confidential.

Strategies that may assist with the informed consent process in the setting of living organ donation include:

- assessment of the donor by a team that is independent from the potential recipient’s care team
- in the absence of a completely separate donor assessment team, the identification of an independent donor advocate
- “cooling-off” periods between the provision of the information and consent, or between consent and the actual surgery
- optimal communication strategies to convey information about the risks and benefits
- consent forms that provide written evidence of full disclosure and understanding leading to informed consent.

It is recognized that difficulties may exist in the provision of a completely independent donor assessment team. In many regions, the number of health care professionals with specialized expertise relevant to the donor assessment is limited; there is a high probability that one or more individuals on the team are also involved in some aspect of recipient assessment or care. This impact of certain issues [i.e., immunologic risk (risk of acute rejection) or technical aspects of the specific donor or recipient surgery] can only be discussed by someone with knowledge of both donor and recipient. Nonetheless, a comprehensive and ethically sound consent process is essential to optimally care for potential living donors and maintain public trust in living donor programs in Canada.

### **Canadian practice:**

The environmental scan of living donor programs conducted prior to the forum revealed that in 61% of programs the organ recipient rarely (n=1) or never (n=10) sees the same medical specialist as the recipient. In two living kidney donor programs, the donor and recipient are always seen by the same nephrologist.

In one liver living donor program, the program reported that it was likely that either the hepatologist or surgeon charged with evaluating the donor was also likely to have been involved in the care of the recipient; this program employed an independent assessment by an internist as an independent donor advocate. A single lung living donor program reported that both the donor and recipient were usually seen by the same respirologist; in this program the donor was also referred to an external respirologist acting as an independent donor advocate.

In 35% of the programs, the donor surgeon always (n=5) or usually (n=1) was involved in evaluating the recipient, while 41% (n=7) indicated this happens sometimes. In some cases, the same surgeon performs both operations.

In terms of an actual written consent form for live donation, only four programs indicated use of a consent form specific to live organ donation. Two programs rely on the coordinator to obtain written consent, and in two the surgeon is responsible.

### **Existing recommendations:**

Consensus Statement of the Amsterdam Forum on the Care of the Live Kidney Donor (Transplantation, 2004): “In order to minimize the appearance of ‘conflicts of interest,’ transplant centers should make efforts to assure that the medical and psychosocial assessments and the decision to donate incorporates health care professional(s) not involved in the care of the recipient. The concept of this recommendation is to provide a health care professional as an advocate for the welfare of the potential donor.

Procedural safeguards should be utilized and explored to minimize coercion and enhance autonomous decision making; for example, by a ‘cooling off period’ and assessment of donor retention of information.”

The US Department of Health and Human Services Advisory Committee on Organ Transplantation (ACOT) has developed examples of both templates for the initial consent to living liver donor evaluation and informed consent for living donor surgery. However, “ACOT does not believe that these or any forms are a substitute for in-person communication between physicians and other involved professionals and the potential donor. These forms should be viewed instead as only the written evidence of discussions leading to informed consent based upon full disclosure.”

## 5. Consent: Living Donation from Individuals < 18 Years of Age

### Canadian practice:

Legislation regarding the ability to consent to living organ donation varies from province to province. In Ontario and Prince Edward Island, the relevant tissue donation legislation sets the age of competence at 16. In British Columbia, Newfoundland and New Brunswick, the age is set at 19. Manitoba legislation sets the default age of consent at 18, although the Manitoba Act also creates a framework that allows individuals as young as 16 to consent, so long as the donation is going to a member of the “immediate family” and there is an independent assessment of capacity (i.e., an assessment by physician with no relationship to the recipient). In Nova Scotia and Saskatchewan no specific age is mentioned; rather any person who has “attained the age of majority” can consent. In Alberta, “any adult person who is mentally competent” may consent, usually interpreted to mean 18 (see, for example, Alberta’s *Age of Majority Act*).

If an individual is competent and meets the age specified in the relevant legislation, they can clearly consent to a live organ donation. It is arguable, however, that the mature minor rule applies. If so, “mature minors” would be capable of providing consent regardless of the age mentioned in the legislation. There is no case law specifically addressing this possibility in Canada.

Although existing law may permit minors and young adults to donate organs, such donations have been rare.

### International practice:

Most US transplant centres in the US regard age < 18 years to be an absolute exclusion criteria for donation (Bia et al., Transplantation, 1995).

A review of the US experience of living donation from 60 individuals < 18 years old (Delmonico et al., Am J Transplant, 2002) revealed that minor donor kidneys were transplanted more frequently to adults than to pediatric recipients. Only 12% of the recipients from minor donors were identical twins.

### Existing Recommendations:

Consensus Statement (JAMA 2000): “Thus, conference participants were generally opposed to live organ donation from a minor [individuals younger than 18 years]. However, exceptional circumstances that would permit the ethical use of a minor as a live donor were established by the conference attendees.”

Report of the Amsterdam Forum on Live Kidney Donation (Transplantation 2005): “Forum participants agreed... that minors less than 18 years of age should not be used as living kidney donors.”

Additional Guidelines on the Use of Minors as Living Kidney Donors by Santiago-Delpin (Am J Transplant 2003;3:1182) which suggested “the limitation, except in identical twins, to donation only if above 16 years of age.”

European Renal Association-European Dialysis and Transplant Association (Nephrol Dial Transplant 2000): Exclusion criteria includes “age < 18 years.”

UK Guidelines for Living Donor Kidney Transplantation (2000): “Individuals under the age of 18 should rarely, if ever, be considered as potential living donors.” British Medical Association: “It is not appropriate for live, non-autonomous donors (minors) to donate non-regenerative tissue or organs.”

## 6. Long-Term Follow-up

Although many have suggested that long-term follow-up of living organ donors is recommended, there is a lack of clarity around the specific responsibilities of the living donor program relative to the family physician, as well as the frequency and duration of follow-up by the donor program.

Important factors to consider in any recommendation regarding long-term follow-up include the distance of the donor from the donor/transplant program, the potential for incurred expenses in traveling to obtain testing or follow-up, the willingness of donors to participate in follow-up testing or appointments, and the work-load of following living donors over the long-term. Some have raised concerns that the requirement for specialized long-term follow-up may negatively impact a donor's perception of their health, adversely affecting their quality of life.

### **Canadian practice:**

According to the environmental scan of living donor programs conducted prior to the forum, considerable variation exists as to the type and frequency of follow-up of living organ donors. The majority of programs provide post-operative follow-up within the first three months after donation, usually by the surgeons and donor coordinators. Although all programs recommended follow-up at one-year post-donation, in only 6 of 18 programs was this provided by either the medical specialist ( $n=4$ ) or surgeon ( $n=2$ ) involved in the donor assessment. In five programs, the donor coordinator provided the one-year follow-up. Thirteen programs request that all donors be followed by their family physicians. In many programs, follow-up was arranged by the donor coordinator by contacting the donor ( $n=10$ ) and/or their family physician ( $n=7$ ) with a written reminder to perform certain investigations annually. Several programs commented that it was up to the donor to initiate follow-up and that the program does not keep track of whether this actually occurred. Few programs ( $n=5$ ) reported that follow-up could continue for more than five years.

An earlier environmental scan of living donor programs in Canada suggested similar findings with only 25% of programs usually or always providing follow-up beyond one year for both medical issues and non-medical issues. This is substantiated by the fact that 72% of 65 Canadian living donors reported that their health was not being followed on a regular basis by a transplant/organ specialist. Forty-nine percent of living donors felt that follow-up should be provided by the program. The lack of sufficient medical and psychosocial follow-up was a common theme in the focus group discussions with living donors that were conducted as part of this environmental scan (Environmental Scan of Policies, Practices, Experiences, Issues and Barriers Related to Live Organ Donation, CCDT, July 2004).

### **International practice:**

In a survey of 28 UK centres, 18 centres arranged life-long follow-up, 7 arranged limited follow-up (usually several years), and 3 centres did not follow donors in the long-term (Lumsdaine et al., Br J Surg, 1999).

In the US, only 13% of UNOS-approved centres recommend indefinite donor follow-up (Bia et al., Transplantation, 1995).

In a French survey, 86% of programs recommended lifelong annual review, with 2/3 of programs assuming this responsibility themselves. Four programs recommended one to five years of follow-up only, indicating that this was preferred such that “the donor status would not be perceived as pathological” (Gabolde et al., Nephrol Dial Transplant, 2001).

In June 2005, the Organ Procurement and Transplantation Network adopted a requirement that American transplant centres report: the death of a living donor (related to organ donation), the return of a living donor to the operating room in the immediate post-operative period, a readmission of a living donor within six months of the procedure, or organ failure requiring a living donor to be placed on the transplant wait-list.

### **Existing recommendations:**

Report of the Amsterdam Forum on Live Kidney Donation (Transplantation, 2005): “As in the general population, based on age and other medical risk factors (e.g., hypertension, proteinuria, hyperlipidemia, impaired glucose tolerance test) kidney donors should undergo regular long-term follow-up of body weight, blood pressure, blood sugar, serum creatinine, and urinalysis.” The report does not recommend who is responsible for conducting long-term follow-up, or for the frequency or duration of follow-up.

European Renal Association-European Dialysis and Transplant Association (Nephrol Dial Transplant, 2000): “Donors should be offered life-long follow-up with check-up examinations once a year.”

UK Guidelines for Living Donor Kidney Transplantation (2000): “It seems reasonable, however, to recommend that donors are evaluated at least annually to measure blood pressure, check their renal function, and examine their urine for proteinuria. Life-long follow-up is recommended. The transplant centre, nephrology unit, or patient’s GP may undertake follow-up.”

### Vancouver Forum 2005 on the Care of Non-renal Living Donors:

1. Lung working group: Recommended that comprehensive short-term follow-up should be mandatory and that long-term follow-up should be strongly encouraged. They recognized that the long-term consequences of donor lobectomy are poorly described in the literature. No clear recommendations were provided regarding follow-up testing, although the following were proposed by some participants: pulmonary function tests, six-minute walk test, chest radiography, quality of life surveys, and psychiatric evaluation.
2. Liver working group: Recommended that live donors be followed for at least one year following liver donation. Suggested that further follow-up may be desirable but not always feasible due to distance. No recommendations regarding specific testing were made.

## 7. Financial Disincentives to Living Donation

Potential donors often express concern about the financial implications of donation, including out-of-pocket expenses incurred during the donor evaluation and with donor surgery, loss of income, and potential risks to current and future insurability.

The magnitude of out-of-pocket expenses for travel and accommodation vary substantially and are affected by a large landmass-to-population ratio such as in Canada. No prospective data exists in Canada to fully quantify the magnitude of these expenses. A Canadian survey of 67 living kidney or liver donors revealed that 74% of donors incurred out-of-pocket expenses ranging in amounts between \$20 and \$6,500. Only 41% reported that they were reimbursed for at least some of their expenses. The same survey reported that 48% of donors suffered a loss of income due to donation; estimates of amounts ranged from \$600 to \$45,000 with an average of \$5,476. The majority (92%) of donors interviewed in this survey indicated that the presence or absence of reimbursement for expenses did not influence their decision to donate (Environmental Scan of Policies, Practices, Experiences, Issues and Barriers Related to Live Organ Donation, CCDT, July 2004). There is insufficient evidence to determine the extent to which financial disincentives have discouraged individuals from pursuing living donation.

### **Canadian practice:**

Canada does not have a unified national strategy to reimburse living organ donors. The maritime provinces have the most comprehensive program to reimburse travel, accommodation and meal expenses, due in large part to the fact that all transplant activity for the region occurs in Nova Scotia. In other jurisdictions, reimbursement for expenses is incomplete and variable. Existing options for partial reimbursement include accessing existing policies (Employment Insurance, Medical Expense Tax Credit), disability insurance, or support from charitable organizations.

All of the relevant provincial legislation prohibits commercial dealings with human tissue. For example, section 10 of Alberta's legislation states "No person shall buy, sell or otherwise deal in, directly or indirectly, for valuable consideration, any tissue for a transplant ..."

Nevertheless, it may be permissible to provide an organ donor with financial reimbursement for expenses incurred. It is unclear, however, what kind of reimbursement would be considered ethically appropriate and just. One of the policy justifications for the ban was to avoid the creation of a financial incentive that might lead to a market and, thus, the exploitation of vulnerable populations. From a consent perspective, the nature of the reimbursement needs to be carefully communicated. Likewise, the potential for coercion should not be underestimated.

### **International practice:**

Three major international organizations (Council of Europe, World Medical Association, American Medical Association's Council on Ethics and Judicial Affairs) have clearly distinguished between commercial trade in organs and remuneration of "out-of-pocket" expenses. In some countries (France, Germany, Japan, Morocco), the transplant centre is responsible for reimbursing travel and accommodations expenses, while in others (Belgium, Spain, Finland, Singapore), the state is responsible. A number of countries have legislation that implicitly or explicitly forbids compensation of any kind to living donors.

**Existing recommendations:**

Consensus Statement (JAMA 2000): “Living organ donors should not personally bear any of the costs associated with donation. In addition, guidelines should be established that are similar to those for short-term disability to defray lost wages.”

Report of the Amsterdam Forum on Live Kidney Donation (Transplantation, 2005): not stated.

European Renal Association-European Dialysis and Transplant Association (Nephrol Dial Transplant, 2000): not stated.

UK Guidelines for Living Donor Kidney Transplantation (2000): “Although it is illegal to offer, give or receive any payment or other benefit from providing a kidney for transplant, donors may be reimbursed for loss of earnings and other expenses (e.g., traveling and subsistence) which are related to the medical evaluation and kidney donor operation. Hospital trusts and health authorities are permitted to reimburse the donor for expenses incurred but are under no obligation to do so. However, it seems reasonable that the health authority paying for the recipient operation should also meet the necessary costs incurred by the donor.”

## **Appendix 3: A Report of the Amsterdam Forum On the Care of the Live Kidney Donor – Data and Medical Guidelines**

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# A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines

Kidney transplant physicians and surgeons met in Amsterdam, The Netherlands, from April 1–4, 2004 for the International Forum on the Care of the Live Kidney Donor. Forum participants included over 100 experts and leaders in transplantation representing more than 40 countries from around the world, including participants from the following continents: Africa, Asia, Australia, Europe, North America, and South America.

(*Transplantation* 2005;79: S53–S66)

The objective of the Forum was to develop an international standard of care with a position statement of The Transplantation Society regarding the responsibility of the community for the live kidney donor. The position statement was adopted by the Council of The Transplantation Society (1).

## The Mission of the Amsterdam Forum

Abdallah Daar presented the mission statement of the Amsterdam Forum emphasizing the concern of the participants for the welfare of the live donor. Specific objectives of the Forum included the development of an international standard of care for the live donor; the development of a position statement regarding the responsibility of the transplant community for the live kidney donor; and the forging of an alliance with the World Health Organization (WHO) to implement these standards. The intent of the Forum leaders was for conference participants to become subsequent emissaries of these standards within their geographical sphere of influence around the world.

## Alliance with the World Health Organization

Carl Groth and Luc Noël provided a background report regarding the involvement of The Transplantation Society with WHO, and the role of the Amsterdam Forum as a continuum of the Madrid WHO conference on organ donation and transplantation in October 2003.

## Preamble

This report of the Amsterdam Forum is derived from an international experience of participants and also from evidence-based recommendations; it is not a document of mandatory regulation. Medical judgment as a reflection of published data and physician experience influences the decision to accept (or not) an individual as a live kidney donor.

## What Is Known Regarding the Sentinel Events of Live Kidney Donors

Forum participants were charged with outlining what is known—and not known—about the sentinel events regarding living donors in the current era (death, dialysis, and need for a kidney transplant), and developing recommendations

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ISSN 0041-1337/05/7900-53  
DOI: 10.1097/01.TP.0000157343.27949.F

for the collection of data to improve the care of potential and actual living donors.

Ahad Ghods and Nasser Simforoosh presented the Iranian experience with live donor outcomes (2). As of 2003, a total of 15,948 renal transplants have been performed in Iran (12,504 living unrelated, 3,049 living related, and 395 deceased donor transplants). With over 15,000 live kidney donors in Iran, the perioperative mortality rate of live kidney donation was 3 in 15,000 (0.02%).

Ingela Fehrman-Ekhholm and Jonas Wadström presented data of the Swedish Registry. With more than 20 years of follow-up, 85% of over 400 kidney donors were alive, whereas the expected survival rate was 66% (3, 4). Survival was 29% better in the donor group than in the comparative cohort.

Arthur Matas submitted data from a survey of 171 United States kidney transplant centers to determine current living donor morbidity and mortality for open nephrectomy, hand-assisted laparoscopic nephrectomy (LN), and non-hand-assisted LN (5). Between January 1, 1999 and July 1, 2001, these centers carried out 10,828 living donor nephrectomies: 52.3% open, 20.7% hand-assisted LN, and 27% non-hand-assisted LN. Two donors (0.02%) died from surgical complications and one is in a persistent vegetative state (all after LN). Reoperation was necessary in 22 (0.4%) open, 23 (1.0%) hand-assisted LN, and 21 (0.9%) non-hand-assisted LN cases ( $P=0.001$ ). Complications not requiring reoperation were reported for 19 (0.3%) open, 22 (1.0%) hand-assisted LN, and 24 (0.8%) non-hand-assisted LN cases ( $P=0.02$ ). Readmission rate was higher for LN (1.6%) versus open (0.6%) donors ( $P<0.001$ ), almost entirely as a result of an increase in gastrointestinal complications in LN donors.

## Long-Term Complications of Donors

Ingela Fehrman-Ekhholm and Jonas Wadström reported upon the glomerular filtration rate (GFR) and the prevalence of hypertension as compared with age- and gender-expected values. In their series of over 400 donors, no accelerated loss of kidney function was observed in live donors who had normal renal function at the time of nephrectomy (4). However, there was deterioration in the renal function of donors with increasing age, similar to what is seen among normal healthy subjects. The average glomerular filtration rate in donors aged 75 years and over was 48 ml/min/1.73 m<sup>2</sup>. A GFR < 30 ml/min was found in five donors. However, three donors developed renal disease, and one was on dialysis treatment. In two of these cases, hereditary factors were possibly involved.

There was no increase in age-specific prevalence of hypertension for female kidney donors. However, one-third of the donors (aged 46–91 years) who had donated more than 20 years ago had hypertension; but the age-adjusted prevalence of hypertension among donors was not higher than in the general population. Significant proteinuria ( $\geq 1.0$  g/L) was found in 3% and slight proteinuria ( $< 1.0$  g/L) in 9% of the donors. Proteinuria was associated with hypertension and a lower GFR.

### Pregnancy after Live Kidney Donation

Annika Tibell and Anders Hartmann concluded that donor nephrectomy is not detrimental to the prenatal course or outcome of future pregnancies. There are no data to suggest that hyperfiltration associated with the combination of unilateral nephrectomy and pregnancy leads to significant hypertension, proteinuria, change in glomerular filtration rate, or abnormalities of the urinary sediment (6, 7). It was recommended, however, to delay pregnancy until at least 2 months after nephrectomy to assess renal compensation prior to conception with evaluation including blood pressure, GFR, and assessment for microalbuminuria. The emphasis was to verify that postpartum renal function is normal.

### Donors Needing Transplants

A total of 56 previous living donors were identified in the database of the United Network for Organ Sharing (UNOS) as having been subsequently listed for deceased donor kidney transplantation, with more than 50,000 live kidney transplants performed since 1987. Of the previous kidney donors, 43 received transplants and 36 had functioning grafts at the time of the published report (8). One patient died after transplantation; two candidates died while waiting on the list. At the time of the donation, the donors ranged in age from 17 to 61, with an average age of 31. The time from donation to listing ranged from 2 to 32 years, with a mean and median of 15 years. At listing, 40% had a diagnosis of hypertensive nephrosclerosis. An additional 17% were listed with focal glomerulosclerosis, and 13% with chronic glomerulonephritis.

Bob Metzger brought to attention a current UNOS policy for live kidney donors that assigns an allocation priority for a deceased donor kidney if the previous live kidney donor subsequently become a candidate for a kidney transplant later in life. However, there was no consensus to develop such a policy internationally. Stephen Munn reported that the New Zealand community has no facility in its cadaver organ allocation system for any such priority provision that was not of medical benefit to the list as a whole. Further, 20% of the live donors in New Zealand are from other countries, some of which have no end-stage renal program. Thus, such an allocation priority for previous donors is not feasible to implement internationally.

### Fifty Years of Live Kidney Donation

Fifty years have elapsed since the first successful kidney transplant from a live donor and a substantial body of published evidence indicates that there is little long-term medical risk to a healthy donor after unilateral nephrectomy. Gil Thiel brought to attention, however, the potential of underreporting donor complications because of the hesitation of the

transplant physicians to reveal them either to the hospital center, future donors, or insurance carriers.

Eduardo Santiago-Delpín stressed the responsibility of transplant centers to assure donor protection, safety, and welfare. Forum participants agreed that prior to donation, the live kidney donor must receive a complete medical and psychosocial evaluation, receive appropriate informed consent, and be capable of understanding the information presented in that process to make a voluntary decision. All donors should have standard tests performed to assure donor safety (1). These include blood and urine screening tests, chest X ray, electrocardiogram, cardiac stress test, radiographic assessment of the kidneys and vessels. A complete listing of tests is appended by Andrew Bradley. Human leukocyte antigen (HLA) typing can be useful to determine an HLA identical sibling; otherwise it is not seemingly vital to a successful outcome (9). Forum participants discussed the evaluation of various medical issues in the potential donor, such as donor hypertension, body mass index, dyslipidemia, renal function, malignancy, and a history or current presence of infectious diseases such as tuberculosis or hepatitis.

As in the general population, based upon age and other medical risk factors (e.g., hypertension, proteinuria, hyperlipidemia, impaired glucose tolerance test), kidney donors should undergo regular long-term follow-up of body weight, blood pressure, blood sugar, serum creatinine, and urinalysis. Abnormalities should be treated promptly by either the local medical physician or the transplant nephrologist. Long-term collaborative prospective studies and comprehensive national registries should be established to determine whether the incidence of medical risk factors and renal dysfunction is different from the general population.

### Donor Hypertension

Hypertension has been considered to be a contraindication in potential renal transplant donors. However, the precise risk to donors who have borderline elevation in blood pressure (BP) and those with a family history of hypertension has not been conclusively determined. Greg Obrador noted that the threshold values for hypertension are different depending on the technique used to measure BP. Ambulatory blood pressure monitoring (ABPM) was reported by Fatma Nurhan Ozdemir to be more accurate than in-office blood pressure measurement (OBPM) in recording true potential donor BP (10, 11).

Gil Thiel reported 18 donors who were hypertensive at the time of nephrectomy. At 7 years following nephrectomy, 10 of the 18 donors were on antihypertensive treatment (five donors with one medication, three donors with two medications, and two donors with three medications). One-third of these 18 donors (hypertensive at donation) were normotensive at 7 years following nephrectomy without any treatment. Thus, hypertension at the time of nephrectomy may have been due to stress conditions before donation. In contrast, among 73 normotensive donors at the time of nephrectomy, only 15 were on antihypertensive treatment (12 donors on one medication, two donors on two medications, and one donor on three medications) at 7 years after nephrectomy. The outcome (renal function) of the 18 donors determined to be hypertensive at nephrectomy was no different than the 75 normotensive donors. At 7 years, the mean estimated creati-

nine clearance for the hypertensive donor group was  $71 \pm 19$  (median 67) ml/min/1.73 m<sup>2</sup>, not statistically different for the initially normotensive group  $75 \pm 17$  (median 73) ml/min/1.73 m<sup>2</sup>.

Mark Stegall reported upon the recent Mayo Clinic experience. The GFR (as determined by iothalamate clearance corrected for body weight) of 25 hypertensive donors was not statistically different than 150 normotensive donors prior to nephrectomy or at 1 year postdonation (12). Blood pressure was easily controlled in hypertensive donors with an angiotensin receptor blocker and diuretics; none had microalbuminuria.

The following consensus guidelines regarding hypertensive donors were adopted following discussion by Greg Obrador, M.K. Mani and Ian Dittmer:

- Patients with a BP  $>140/90$  by ABPM are generally not acceptable as donors.
- BP should preferably be measured by ABPM, particularly among older donors ( $>50$  years) and/or those with high office BP readings.
- Some patients with easily controlled hypertension who meet other defined criteria (e.g.,  $>50$  years of age, GFR  $>80$  ml/min, and urinary albumin excretion  $<30$  mg/day) may represent a low-risk group for development of kidney disease after donation and may be acceptable as kidney donors.
- Donors with hypertension should be regularly followed by a physician.

## Obesity

Gabriel Danovitch and Jose Morales led the discussion on live obese kidney donors. Obesity was defined by a body mass index (BMI) of  $> 30$  kg/m<sup>2</sup>. All potential donors should have BMI determined at initial evaluation. Evaluation should also include other comorbidities associated with obesity such as microalbuminuria, impaired GTT, hypertension, hyperlipidemia, cardiovascular disease, sleep apnea, and liver disease.

Obesity should be considered an increased risk for renal disease; however, there is no data on the outcome of such individuals. Jose Morales commented upon patients who underwent unilateral nephrectomy for reasons other than donation, noting an increased risk for proteinuria and renal insufficiency on long-term follow-up if the BMI was  $\geq 30$  (13). However, Mark Stegall reported that renal function of more than 100 obese donors ( $\geq 30$  BMI) after donation was no different from that of nonobese donors. Further, the corrected GFR of obese donors was greater than that of nonobese donors, and the morphology of biopsied obese donor kidneys (particularly glomerular volume) is no different from nonobese donors. The selection criteria for all donors at the Mayo Clinic were the same by a corrected GFR  $>80$  ml/min/BSA; normal urinary protein and albumin secretion, and fasting blood glucose  $<126$  mg/dl (for fasting glucose 100–125, a 2-hour GTT is recommended). Finally, in the Mayo experience, hand-assisted donor nephrectomy is safe in obese donors.

The following consensus guidelines were adopted regarding obesity:

- Patients with a BMI  $>35$  kg/m<sup>2</sup> should be discouraged from donating, especially when other comorbid conditions are present.
- Obese patients should be encouraged to lose weight prior to kidney donation and should be advised not to donate if they have other associated comorbid conditions.
- Obese patients should be informed of both acute and long-term risks, especially when other comorbid conditions are present.
- Healthy lifestyle education should be available to all living donors.

## Dyslipidemia

Arturo Dib-Kuri noted that various types of dyslipidemia have been associated with decreased kidney function in the general population and with faster rates of progression in patients who have chronic kidney disease. Dyslipidemia should be included along with other risk factors in donor risk assessment, but dyslipidemia alone does not exclude kidney donation.

## Acceptable Donor Renal Function

Robert Gaston and Mario Abbud-Filho led the discussion on the level of renal function that defines an acceptable living kidney donor. Individuals contemplating donor nephrectomy should demonstrate "normal" renal function as determined by assessment of GFR. The definition of "normal" GFR changes with age, as renal function deteriorates over time (14–16). Carl Cardella noted a decrease in GFR of approximately 1 ml/min/1.73 m<sup>2</sup> per year after age 40. There is a documented acute decrease in GFR of approximately 30% after unilateral nephrectomy; however, the impact of unilateral nephrectomy on this rate of decline in GFR is unknown.

All potential kidney donors should have GFR estimated. Creatinine based methods may be used to estimate the GFR; however, creatinine clearance (as calculated from 24-hour urine collections) may under- or overestimate GFR in patients with normal or near normal renal function (17). Calculated GFR values (Modification of Diet in Renal Disease [MDRD], Cockcroft-Gault) are not standardized in this population and may overestimate GFR. These methods may be replaced or supplemented by isotopic estimation of GFR (e.g., iothalamate, 99-technetium clearances) in cases of borderline GFR determination.

Jaime Herrera-Acosta noted that some might have difficulty in obtaining <sup>125</sup>Iothalamate clearance, for which his center substitutes creatinine clearances obtained during mild water diuresis and short-term urine collections to make sure that urine flows were exact. An excellent correlation of creatinine clearance with simultaneous <sup>125</sup>Iothalamate clearance was achieved in 46 kidney donors ( $r=0.84$ ,  $P<0.0001$ ).

Acceptable GFR in a donor is that which can be predicted to provide adequate GFR for both donor and recipient after donor nephrectomy/transplantation. Robert Gaston and Mario Abbud-Filho cited reports of the literature that reveal donors with GFR  $\leq 80$  ml/min before nephrectomy cannot be reliably expected to provide or maintain optimal function after nephrectomy, although as many as 20% of U.S. transplant centers would accept a creatinine clearance as low as 60 ml/min (18, 19).

Dan Brennan noted that donors who are thin, small, and female with a creatinine clearance of  $<80$  ml/min and normalized for body surface area (BSA) could alternatively be normalized for height and a more accurate GFR can be determined. An average-sized 60-year-old person (70 kg body weight) with a serum creatinine of 1.0 mg/dl can be presumed to have a GFR of 80 ml/min (20).

Bernardo Rodríguez-Iturbe commented that if donors are challenged with a creatinine load, they might not normally increase the tubular secretion of creatinine (revealing an impaired tubular functional reserve) (21).

The following consensus guideline was adopted regarding acceptable renal function: a GFR  $<80$  ml/minute or 2 standard deviations below normal (based on age, gender, and BSA corrected to  $1.73/\text{m}^2$ ) generally preclude donation. Kidneys from live donors with GFR  $\leq 80$  ml/min are associated with relative risk of graft loss of 2.28 compared to those with greater prenephrectomy GFR (22). However, successful transplantation was noted from some, usually elderly, living donors with GFR as low as 65–70 ml/min, indicating a need for individualization and careful follow-up of donors with GFR of  $<80$  ml/min/ $1.73/\text{m}^2$ .

### **Urine Analysis for Protein and Blood**

The discussion was initiated by M.K. Mani and Yves Vanrenterghem. Proteinuria is a marker of glomerular pathology and renal disease. Proteinuria should be assessed as a standard part of the donor work up. Dipstick urinalysis for proteinuria and hematuria has been used to screen renal disease, but Gil Thiel suggested that dipstick measurements of proteinuria are not adequate in the assessment of a potential donor. Laboratories vary as to normal values of quantitated urine protein, but a consensus was reached to conclude that a 24-hour urine protein of  $>300$  mg is a contraindication to donation.

The significance of microalbuminuria has been studied mostly in patients with diabetes mellitus. However, even in non-diabetics, it may be the first sign of a glomerular pathology. Gil Thiel suggested that kidney donors merit a screening and follow-up with microalbuminuria measurement (23). Albumin and protein concentration in urine should be referenced to either a time-collected specimen or to urinary creatinine concentration. A level of 5 mg (u-albumin/mmol u-creatinine) in a morning urine specimen represents approximately 50 mg albumin/24 h urine. M.K. Mani suggested, however, that the assessment of microalbuminuria is more expensive to perform and has not been well established in all parts of the world. A concern regarding laboratory consistency and accuracy was expressed.

Thus, Forum participants concluded that microalbuminuria determination may be a more reliable marker of renal disease, but its value as an international standard of evaluation for kidney donors has not been determined.

The discussion of hematuria was initiated by Kazuhide Saito and commented upon by Osman Alfurayh. Isolated microscopic hematuria (defined as  $>3\text{--}5$  urinary sediment red blood cells (RBCs)/HPF) may not be a contraindication to donation. RBCs with glomerular origin have a dysmorphic appearance observed by phase-contrast microscopy and automated RBC analysis. Patients with persistent microscopic hematuria should not be considered for kidney donation unless urine cytology and a complete urologic work up are per-

formed. If urological malignancy and stone disease are excluded, a kidney biopsy may be indicated to rule out glomerular pathology such as IgA nephropathy.

Dan Brennan cited a recent report from Japan describing the presence of latent mesangial IgA deposits in approximately 16% of biopsies obtained at the time of transplantation from both living and deceased donors otherwise considered healthy (24). In some of the affected individuals, these findings were associated with a mild degree of microhematuria, mesangial proliferation, and glomerular macrophage infiltration, especially with combined IgA and C3 deposition.

### **Diabetes**

The risk of the donor developing diabetic nephropathy following kidney donation was discussed by Connie Davis and Ed Cole. Diabetes is associated with an increased risk of postsurgical complications and future development of renal failure compared to the general population. Data by Silveiro et al. (25) were referenced to suggest that a nephrectomy in a patient with Type 2 diabetes might increase the progression of disease. Further, the prevalence of microalbuminuria is increased after nephrectomy.

Individuals who are at risk for developing Type 2 diabetes include those with a familial history, a BMI of  $>30 \text{ kg}/\text{m}^2$ , woman with gestational diabetes, and excessive alcohol use. The following guideline was developed: individuals with a history of diabetes or fasting blood glucose  $\geq 126$  mg/dl (7.0 mmol/L) on at least two occasions (or 2-hour glucose with OGTT  $\geq 200$  mg/dl (11.1 mmol/L)) should not donate.

### **Stone Disease**

Fernando Gabilondo and Mahendra Bhandari led the discussion of stone disease. Patients with lithiasis should be screened for metabolic stone forming abnormalities. Kidneys have been transplanted knowingly containing a renal stone (26, 27).

An asymptomatic potential donor with history of a single stone may be suitable for kidney donation if:

- No hypercalciuria, hyperuricemia, or metabolic acidosis.
- No cystinuria or hyperoxaluria.
- No urinary tract infection.
- Multiple stones or nephrocalcinosis are not evident on computed tomography (CT) scan.

Younger patients have a longer exposure to risk of recurrence. The risk of recurrence after any single stone is difficult to predict in any individual. The younger the donor age (age 25–35), the longer the exposure to the possibility of a recurrence (28).

Asymptomatic potential donor with current single stone may be suitable if:

- The donor meets the criteria shown previously for single stone formers, and current stone is  $<1.5$  cm in size or potentially removable during transplant.

Ex vivo ureteroscopy is a technically feasible means of rendering a stone-bearing kidney stone free, without compromising ureteral integrity or renal allograft function (29). It is not known whether stone formers who donate a kidney

have worse outcomes with respect to renal function compared to stone formers with two kidneys. However, a recurrent stone may not affect the function of a remaining kidney if it is carefully monitored (30).

Stone formers who should not donate are those with: 1) nephrocalcinosis on X ray or bilateral stone disease; and 2) stone types that have high recurrence rates and are difficult to prevent, such as:

- Cystine stones that have a high rate of recurrence and a need for urologic procedures in the donor.
- Struvite stones or infection stones that are difficult to eradicate and thus not feasible to transplant them into an immunosuppressed patient.
- Stones associated with inherited or other systemic disorders, such as primary or enteric hyperoxaluria, distal renal tubular acidosis, and sarcoid, because of the probability of a high rate of recurrence and the risk of renal insufficiency.
- Stones in the setting of inflammatory bowel disease with an increased risk of stones particularly after bowel resection, also increased risk of renal insufficiency.
- Recurrence while on appropriate treatment (i.e., failed therapy).

### **History of Donor Malignancy**

Jeremy Chapman and Domingo Casadei led the discussion of donor malignancy. Living kidney donors should be screened by standard medical guidelines to exclude malignancy, noting that:

- The risk of clinical and subclinical malignancy increases markedly with age, especially over 50 years.
- The risk of different cancers differs between countries.
- Donors with low-grade nonmelanoma skin cancer may be accepted; otherwise the living kidney donor should be free of current or untreated malignancy.

A prior history of the following malignancies usually excludes live kidney donation:

- Melanoma, testicular cancer, renal cell carcinoma, choriocarcinoma, hematological malignancy, bronchial cancer, breast cancer and monoclonal gammopathy (31–34).

A prior history of malignancy may only be acceptable for donation if:

- Prior treatment of the malignancy does not decrease renal reserve or place the donor at increased risk for end-stage renal disease (ESRD).
- Prior treatment of malignancy does not increase the operative risk of nephrectomy.

A prior history of malignancy usually excludes live kidney donation but may be acceptable if:

- The specific cancer is curable and the potential transmission of the cancer can reasonably be excluded. Examples include: colon cancer (Dukes A, >5 years ago), non-melanoma skin cancer, or carcinoma in situ of the cervix.

Consent to receive a renal transplant must include a discussion with the donor and the recipient that transmission of malignant disease cannot be completely excluded.

### **Screening for Infectious Disease**

Essam Elsawy led the discussion of donor screening to prevent transmissible infectious disease through live kidney transplantation.

#### **HIV**

The detection of a positive human immunodeficiency virus (HIV-1 and HIV-2) by an ELISA assay for both antigen and antibody in a potential kidney donor should be confirmed by a neutralization test and a western blot analysis. The positive result rules out an individual from being a live kidney donor.

#### **HTLV 1**

If human T-lymphotropic virus (HTLV) 1 is transmitted from a live kidney donor, the recipient may be at risk for the development of T cell leukemia and neurological disorders such as a subacute myelopathy or spastic paraparesis (35). The ELISA test identifies HTLV 1 and 2, but does not distinguish either. Polymerase chain reaction (PCR) is needed to differentiate. The risk for HTLV 2 infection is unknown; it is detected in intravenous drug users.

HTLV is endemic in the West Indies and Japan. Norio Yoshimura presented his personal experience of a recipient developing T cell leukemia from a donor who was HTLV positive; this complication has also been reported from blood transfusion (36). Therefore, HTLV has been included in the routine screening (Table 1) assembled by Dr. Bradley. However, Dan Brennan suggested that the disease is rare in other parts of the world, and testing for its detection in live kidney donors is not routinely done.

#### **CMV and EBV**

Essam Elsawy screens for cytomegalovirus (CMV) IgM to evaluate recent infection, because CMV-reactive IgG is detected in more than 90% positive of his donors. If the CMV IgM is positive, a PCR for CMV is performed. If the PCR is positive, Essam Elsawy excludes live kidney donation until PCR becomes negative. If the CMV IgM positive and PCR are negative, they proceed with transplantation.

Bill Harmon suggested that a living donor (e.g., a parent) who is either CMV or Ebstein-Barr virus (EBV) positive is still acceptable for a recipient who is CMV or EBV negative.

Most of the adults are EBV and CMV positive; most of the children are EBV negative and many are CMV negative. Gil Thiel and Peter Morris expressed a concern that the incidence of posttransplantation lymphoproliferative disorder (PTLD) is rising in pediatric recipients. Approximately 5% of infants who receive living donor transplants develop PTLD, in part because of the intensity of immunosuppression, but also in the circumstance of an EBV positive donor transplant to a negative recipient. The possibility of EBV vaccination of the recipient was discussed by Ian Dittmer. Alternatively, another parent or a relative within the family might be evaluated to determine if they are either EBV (or CMV) negative. Despite these efforts, the importance and success of a live donor

**TABLE 1.** Routine screening for the potential living kidney donor

Urinalysis
Dipstick for protein, blood and glucose
Microscopy, culture and sensitivity
Measurement of protein excretion rate
Assessment of renal function
Estimation/measurement of GFR
Blood tests
Hematological profile
Complete blood count
Hemoglobinopathy (where indicated)
Coagulation screen (PT and APTT)
G6PD deficiency (where indicated)
Biochemical profile
Creatinine, urea, and electrolytes
Liver tests
Urate
Fasting plasma glucose
Bone profile
Glucose tolerance test (if fasting plasma glucose >6–7 mmol/l)
Blood lipids
Thyroid function tests (if indicated)
Pregnancy test (if indicated)
PSA (if indicated)
Virology and infection screen
Hepatitis B and C
Toxoplasma
Syphilis
HIV and HTLV 1/2
Malaria (where indicated)
Cytomegalovirus
Trypanozome cruzi (where indicated)
Epstein-Barr virus
Schistosomiasis (where indicated)
HHV8 and HSV (where indicated)
Strongyloides (where indicated)
Typhoid (where indicated)
Brucellosis (where indicated)
Cardiorespiratory system
Chest X-ray
Electrocardiogram
Stress test
Echocardiography (where indicated)
Assessment of renal anatomy
Appropriate imaging investigations should allow confirmation of the presence of two kidneys of normal size and enable abnormalities of the collecting system and calcification or stone disease in the renal tract to be detected. They must also delineate the anatomy of the renal vasculature.

PSA, prostate-specific antigen; HIV, human immunodeficiency virus; HTLV, human T-lymphotropic virus; HHV, human herpes virus; HSV, herpes simplex virus.

parental transplant was sufficient to not prohibit the use of a CMV or EBV positive donor for a recipient who is CMV or EBV negative.

### Hepatitis C Virus

If the donor has normal liver function tests and the serology test for hepatitis C virus (HCV) is negative (nonreactive antibody determination by ELISA), there is no contraindication for donation. However, if the serology test is pos-

itive for HCV, Essam Elsawy recommended that the recipient HCV status be evaluated. If the potential recipient is negative for HCV, the potential positive HCV donor should be excluded. If the potential recipient is also positive for HCV, the potential donor should be assessed by PCR for HCV. If the potential donor is PCR positive, the potential donor should be excluded because of the risk of HCV transmission to the recipient and because the potential donor may have chronic hepatitis (and is not well). If the potential donor is negative by PCR, the potential donor may not necessarily be excluded because the likelihood of transmission of HCV through the kidney is remote.

Nevertheless, Jose Morales expressed concern regarding HCV superinfection if a different HCV genotype of a positive donor is transmitted to a recipient. The Spanish group has transplanted kidneys from deceased donors with HCV reactivity to HCV positive recipients, but they have not performed live kidney transplantation from HCV positive donors (37). Further, Chakko Jacob and Nabil Mohsin questioned the justification of removing a kidney from a patient who in the future may develop an HCV-associated renal disease. However, Stephen Munn suggested that if certain HCV genotypes (genotype 4) are treated and eradicated in the donor, the potential donor could be reconsidered (if no evidence of chronic hepatitis or cirrhosis on biopsy).

### Hepatitis B Virus

The detection of hepatitis B surface antigen (HBsAg) in a potential donor generally excludes the individual from live kidney donation (38). However, Stephen Munn reported that in New Zealand, some of the live kidney donors have been hepatitis B virus (HBV) core antibody positive. An IgM core positive result indicates a recent exposure to the HBV; in contrast, a surface antibody positive result indicates that months may have elapsed since the hepatitis infection. Even if HBsAg is negative, screening for HBV core total antibody (IgM and IgG) should be done to exclude low-level HBsAg and escape mutants of HBV not detectable by the current screening assays for HBsAg.

The ELISA core antibody test can distinguish between IgM and IgG reactivity. If the core antibody result is positive for IgM, a delay in the consideration of the potential donor was recommended to determine whether HBV infection might be progressing. A PCR quantitation of HBV DNA should be performed as appropriate care of the donor. Otherwise, by the New Zealand practice, if the potential donor is PCR negative for HBV, kidneys may be transplanted safely from either an HBV surface antibody positive donor or a donor who is HBV core antibody (IgG) positive into recipients who either have successfully recovered from hepatitis B infection or been immunized against hepatitis B.

### Human Herpes Virus 8

Human Herpes Virus 8 (HHV8) has been shown to induce Kaposi sarcoma and can be transmitted by organ transplantation (39). Gil Thiel mentioned an ongoing research project of screening donors and recipients for HHV8 in Switzerland, but there is no world wide routine screening of live donors for HHV8.

**TABLE 2. Amsterdam Forum Guidelines**

## Donor evaluation

Prior to donation, the live kidney donor must receive a complete medical and psychosocial evaluation, receive appropriate informed consent, and be capable of understanding the information presented in that process to make a voluntary decision. All donors should have standard tests performed to assure donor safety.

## Hypertension

Patients with a BP  $>140/90$  by ABPM are generally not acceptable as donors.

BP should preferably be measured by ABPM, particularly among older donors ( $>50$  years) and/or those with high office BP readings.

Some patients with easily controlled hypertension, who meet other defined criteria, e.g.  $>50$  years of age, GFR  $>80$  ml/min, and urinary albumin excretion  $<30$  mg/day may represent a low-risk group for development of kidney disease after donation and may be acceptable as kidney donors.

Donors with hypertension should be regularly followed by a physician.

## Obesity

Patients with a BMI  $>35$  kg/m $^2$  should be discouraged from donating, especially when other comorbid conditions are present.

Obese patients should be encouraged to lose weight prior to kidney donation and should be advised not to donate if they have other associated co-morbid conditions.

Obese patients should be informed of both acute and long-term risks, especially when other comorbid conditions are present.

Healthy lifestyle education should be available to all living donors.

## Dyslipidemia

Dyslipidemia should be included along with other risk factors in donor risk assessment, but dyslipidemia alone does not exclude kidney donation.

## Acceptable donor renal function

All potential kidney donors should have GFR estimated.

Creatinine based methods may be used to estimate the GFR; however, creatinine clearance (as calculated from 24-hour urine collections) may under or overestimate GFR in patients with normal or near normal renal function.

Calculated GFR values (MDRD and Cockcroft-Gault) are not standardized in this population and may overestimate GFR.

A GFR  $<80$  ml/min or 2SD below normal (based on age, gender, and BSA corrected to 1.73/m $^2$ ) generally precludes donation.

## Urine analysis for protein

A 24-hour urine protein of  $>300$  mg is a contraindication to donation.

Microalbuminuria determination may be a more reliable marker of renal disease, but its value as an international standard of evaluation for kidney donors has not been determined.

## Urine analysis for blood

Patients with persistent microscopic hematuria should not be considered for kidney donation unless urine cytology and a complete urologic work up are performed. If urological malignancy and stone disease are excluded, a kidney biopsy may be indicated to rule out glomerular pathology, such as IgA nephropathy.

## Diabetes

Individuals with a history of diabetes or fasting blood glucose  $\geq 126$  mg/dl (7.0 nmol/l) on at least two occasions (or 2-hr glucose with OGTT  $\geq 200$  mg/dl (11.1 mmol/l) should not donate.

## Stone Disease

An asymptomatic potential donor with history of a single stone may be suitable for kidney donation if:

No hypercalcemia, hyperuricemia, or metabolic acidosis.

No cystinuria, or hyperoxaluria.

No urinary tract infection.

If multiple stones or nephrocalcinosis are not evident on CT.

An asymptomatic potential donor with a current single stone may be suitable if:

The donor meets the criteria shown previously for single stone formers and current stone

$<1.5$  cm in size, or potentially removable during the transplant.

Stone formers who should not donate are those with:

Nephrocalcinosis on x ray or bilateral stone disease.

Stone types with high recurrence rates, and are difficult to prevent (see text).

## Malignancy

A prior history of the following malignancies usually excludes live kidney donation:

Melanoma, testicular cancer, renal cell carcinoma, choriocarcinoma, hematological malignancy, bronchial cancer, breast cancer and monoclonal gammopathy.

A prior history of malignancy may only be acceptable for donation if:

Prior treatment of the malignancy does not decrease renal reserve or place the donor at increased risk for ESRD.

Prior treatment of malignancy does not increase the operative risk of nephrectomy.

A prior history of malignancy usually excludes live kidney donation but may be acceptable if:

The specific cancer is curable and potential transmission of cancer can reasonably be excluded.

## Urinary tract infections

The donor urine should be sterile prior to donation; asymptomatic bacteria should be treated per donation.

Pyuria and hematuria at the proposed time of donation is a contraindication to donation.

Unexplained hematuria or pyuria necessitates evaluation for adenovirus, tuberculosis, and cancer. Urinary tuberculosis or cancer are contraindications to donation.

## Live unrelated donors

The current available data suggest no restriction of live kidney donation based upon the absence of an HLA match. An unrelated donor transplant is equally successful to the outcome achieved by a genetically related family member such as a parent, child, or sibling, who is not HLA identical to the recipient.

## Determination of cardiovascular risk

The clinical predictors of an increased perioperative cardiovascular risk (for non-cardiac surgery) by the American College of Cardiology/American Hospital Association standards fall into 3 categories: major, intermediate, minor.

All major predictors: unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease are contraindications to live kidney donation.

Most of the intermediate predictors: mild angina, previous myocardial infarction, compensated or prior heart failure, diabetes mellitus are also contraindications to donation; Minor predictors: older age, abnormal ECG, rhythm other than sinus, low cardiac functional capacity, history of stroke or uncontrolled hypertension warrant individual consideration.

## Assessment of pulmonary issues

A careful history and physical examination are the most important parts of assessing risk.

Routine preoperative pulmonary function testing (PFT) is not warranted for potential live kidney donors unless there is an associated risk factor such as chronic lung disease.

Increased risk of post operative pulmonary complication is assoc with an FEV1  $<70\%$  or FVC  $<70\%$  of predicted, or a ratio of FEV1/FVC  $<65\%$ .

## Smoking cessation and alcohol abstinence

Smoking cessation at least 4 weeks prior to donation is advised based on recommendations for patients undergoing elective surgical procedures.

Cessation of alcohol abuse defined by DSM-3: 60 gm of alcohol/day sustained over  $\geq 6$  months should be avoided for a minimum of 4 weeks to decrease the known risk of postoperative morbidity.

BP, blood pressure; ABPM, ambulatory blood pressure monitoring; GFR, glomerular filtration rate; BMI, body mass index; BSA, body surface area; CT, computed tomography; ESRD, end-stage renal disease; HLA, human leukocyte antigen.

### Tuberculosis

Essam Elsawy presented the following information regarding tuberculosis. Active *Mycobacterium tuberculosis* infection is a contraindication for donation because tuberculosis has been transmitted from live kidney donors to their recipients (40). Further, a past history of pulmonary tuberculosis is relative contraindication to donation. However, there were instances reported by Forum participants where individuals with history of treated pulmonary tuberculosis have donated a kidney.

Enrique Ona presented that many of the Philippine live kidney donor population may have fibrosis of the lung apex, which radiologists read as evidence of a past tuberculous infection by this "primary complex." The radiologist's evaluation is important to determine active infection by a comparative current chest x-ray with a previous one (if available). They are accepted as donors if it is proven that they don't have an active pulmonary infection and after it is shown that they don't have genitourinary tract tuberculosis. If active pulmonary infection is suspected, the donors are treated (as are most of the recipients) with prophylactic isoniazid (INH) for about 4 months. Thus, a potential donor with a past history of pulmonary tuberculosis who has received adequate treatment may still be an acceptable donor if there is no renal infection. Enrique Ona suggested that donors treated for pulmonary tuberculosis require a more specific and extensive examination of the urinary tract and the kidneys prior to donation.

Pyuria or an anatomical defect on renal ultrasound or intravenous pyelogram (IVP) may be indicative of donor urinary tract infection with tuberculosis. Urinary tuberculosis is contraindication for donation. Essam Elsawy suggested that donors previously treated for urinary tuberculosis might have dormant tuberculosis within the kidney, and thus remain unsuitable for donation. Further, tuberculous pyelonephritis usually results in a decreased GFR of the diseased kidney, making it unsuitable for donation.

M.K. Mani presented the following information. Urinary culture for tuberculosis is not done routinely as it is a poor screening tool; however, the potential donor is usually assessed for pyuria and anatomical radiographic abnormalities of the urinary tract and kidneys, despite a normal chest X ray. Mahendra Bhandari concurred to report in his experience that genitourinary tuberculosis might exist without chest X ray evidence. Finally, in some regions of the world (from Fernando Gabilondo and Nasser Simforoosh), a purified protein derivative (PPD) skin test of tuberculosis is still used to screen potential kidney donors, even though some of the donors may have been vaccinated with Bacille Calmette-Guerin (BCG), a genetically-altered tubercular bacteria rendered avirulent. However, in Egypt, Essam Elsawy noted that BCG vaccination is mandatory for all the population from birth. A positive PPD on that basis may not be helpful to screen a potential live kidney donor. In New Zealand, neither Stephen Munn nor Ian Dittmer screens their donors with a PPD.

### Syphilis

Donors should be screened for syphilis (*Treponema pallidum*) with the rapid plasma reagin (RPR) or Venereal Disease Research Laboratory (VDRL) slide test. The RPR and the older VDRL test detect reactive antibodies. There are sev-

eral conditions that may cause a false positive test: HIV, Lyme disease, mycoplasma pneumonia, malaria, and systemic lupus erythematosus. Therefore, these screening tests, if found to be positive, must be confirmed by a more specific test for syphilis such as a fluorescent treponemal antibody (FTA) absorption test. Donors with a positive confirmatory FTA should be treated according to stage and donation should be delayed until successful treatment is accomplished. There may be a risk of syphilis transmission if the donor is untreated (41). The recipient could receive treatment following transplantation, if there is an urgent need to perform transplant. Secondary syphilis is associated with reversible renal disease.

### Chagas Disease

Chagas disease is endemic in parts of Central and South America and Mexico, where an estimated 16–18 million people are infected with *Trypanosoma cruzi* (42). Trypanosomiasis has been transmitted to kidney transplant recipients from an infected donor (43). Donors from endemic areas should be screened by serologic tests (there are at least three of them). A complement fixation test (Machado-Guerreiro reaction) becomes positive in the acute stage at one month postinfection and remains positive thereafter. The Machado-Guerreiro has a low sensitivity and specificity that yields high incidence of false positives and negatives. The precipitin test (hemagglutination reaction) is 95% positive in the early stages. The immunofluorescence and ELISA tests are highly sensitive and specific, although false-positive reactions occur with malaria, leprosy, and leishmaniasis. If two of the screening tests are positive, the detection of the trypanosome should be ruled out in the blood by a xenodiagnostic test that entails the following: uninfected laboratory-raised insects are fed on a patient, and then examined 30 days later for metacyclic trypanosomes in their hindgut or feces. If positive, the potential donor must be treated and cannot donate until parasitemia turns negative. Otherwise, Mario Abbud-Filho, José Medina-Pestana, and Domingo Casadei suggested that there is no contraindication to live kidney donation from a serology positive donor. In a referenced report by Sousa, nine recipients of kidneys were obtained from Chagas seropositive donors among 239 kidney transplants between 1992 and 1997 (43). All were treated with benznidazole (5 mg/kg/d) for 14 days. None of them experienced acute Chagas disease or seroconversion even after 10 years follow-up. The Forum participants concluded that donors with positive serology for Chagas disease should not be excluded.

### Schistosomiasis

Essam Elsawy suggested that uncomplicated bilharziasis of living kidney donors does not adversely affect either the function or the morphology of the remaining kidney, provided that the donor had functionally and morphologically intact kidneys and bilharzia was treated before donation. There has been no significant difference between bilharzial and nonbilharzial renal transplants in graft function and incidence of graft rejection after 10 years of follow up (44). Nabil Mohsin posed a question regarding the routine treatment of schistosomiasis in an asymptomatic donor who resides in an endemic area. Essam Elsawy replied that treatment is not given unless the donor has an active infection. If there is active schistosomiasis in an otherwise healthy donor, the do-

nor is treated at least one month before transplantation by combined antischistosomal drugs (praziquantel and oxamniquine). Cure without impairing renal function has been observed without a negative impact on the transplant outcome.

### **Strongyloides**

Larvae of *Strongyloides stercoralis* penetrate the skin or mucosa from fecally contaminated soil, are carried by the blood stream to the lungs, break into the alveoli, ascend, are swallowed, and then reach the small intestine. The female worms produce larvae parthenogenically (without fertilization), and the larvae are passed in the host's feces. The presence of nematode larvae in a fecal sample is characteristic of strongyloidiasis; however, an ELISA assay is available for serological detection of strongyloides. Potential donors should be screened for strongyloides in endemic areas because strongyloides has been transmitted via a kidney transplant (45).

### **Brucellosis**

Brucellosis is derived from the bacteria of the genus *Brucella*, primarily passed among animals and acquired by humans from contact with animals or animal products that are contaminated with these bacteria. Brucellosis has been transmitted to recipients of bone marrow transplants (46). Nasser Simforoosh suggested that a patient successfully treated for brucellosis infection may still be a suitable live kidney donor.

### **Malaria**

Malaria has been transmitted from an organ donor to multiple transplant recipients, resulting in the death of a heart transplant recipient (47). Potential live kidney donors who either reside or have traveled to endemic areas should be screened for *Plasmodium falciparum*. Automated hematology analyzers have been used to detect malarial parasites in peripheral blood samples.

### **Urinary Tract Infections**

The donor urine should be sterile prior to donation. Pyuria and hematuria at the proposed time of donation is a contraindication to donation. Asymptomatic bacteruria should be treated predonation. Unexplained hematuria or pyuria necessitates evaluation for adenovirus, tuberculosis, and cancer. Urinary tuberculosis and cancer are contraindications to donation.

Essam Elsawy presented the following information. A history of recurrent cystitis is not a contraindication to donation from a healthy young female; however, unexplained recurrent pyelonephritis is a contraindication to donation. Persistent infection (same pathogen recurs after treatment) warrants anatomic evaluation of urinary tract by upper tract study (IVP, CT scan) and cystoscopy. In men, persistent infection may be associated with chronic bacterial prostatitis. There is no association of renal infection with chronic bacterial prostatitis.

Recurrent urinary tract infection from childhood may indicate reflux and potential donors should undergo a voiding cystourethrogram (VCUG) and an upper tract study. Donation is contraindicated until anatomical cause is ruled out.

### **Blood Donor Regulation and Organ Donor Screening**

Stephen Munn and Carl Cardella noted blood donor services in North America, Australia, and New Zealand have precluded individuals from donating blood if they resided in the United Kingdom during the bovine spongiform encephalopathy (BSE) risk period (during the 1980s and early 1990s) and ate meat (48). Chris Rudge also reported that the U.K. national blood service has issued an instruction to not permit blood donation from anybody who has received a blood transfusion within the last 24 years. Andrew Bradley suggested that, for live kidney donation, the remote risk could be discussed with a prospective recipient and they could accept that risk or not. In contrast, the donor of a blood transfusion is usually to an anonymous recipient. Chris Rudge agreed that regulations for blood and tissues should not apply to organs because the risk/benefit ratio is different, citing the example of screening for HTLV and variant for Creutzfeld-Jacob disease (v-CJD). The conclusion of the Forum participants was that a center transplanting a kidney from a live donor who falls into at-risk categories for v-CJD (residency in the U.K. or a family history of unexplained neurodegenerative disease) has a responsibility to explain the possibility of transmission to the recipient. Nevertheless, the risk is likely to be extremely low and not prohibit live donor kidney transplantation.

### **Live Unrelated Donors**

In Mexico and some European countries, unrelated kidney transplantation is currently illegal. Enrique Ona posed the following question to participants: "Since live donors are more commonly done in the Philippines, what is a minimum HLA-DR antigen match acceptable for transplantation? Blood relation in our part of the world extends to distant relatives and not just from siblings, parents or children. The same is true with the adoption of incentives, gifts, or gratitudinal reciprocity to the donation process which can easily be misconstrued as 'commercialization' or sale."

Chris Rudge presented data from the U.K. evaluating the degree of HLA match in transplants from different donor types and the influence of HLA match on the outcome of all living donor transplants in the U.K. (49). Transplants from unrelated living donors were significantly less well matched. There were two HLA-DR mismatches in 41% of living unrelated donor transplants but less than 5% in living related donor transplants. Nevertheless, there were no significant differences in one-year transplant survival between the two living donor transplant groups.

Francis Delmonico presented current U.S. data that examined whether HLA matching influences the outcome of living donor kidney transplants. Among living unrelated donor transplant recipients, there was no independent effect of DR matching on graft survival, as indicated by 5-year survival rates of 86% (reference group), 85% ( $P=0.85$ ) and 84% ( $P=0.64$ ) for zero, one, and two HLA-DR mismatched grafts, respectively.

Thus, the current available data suggest no restriction of live kidney donation based upon the absence of an HLA match. An unrelated donor transplant is equally successful to the outcome achieved by a genetically related family member such as a parent, child, or sibling who is not HLA identical to the recipient.

### Live Donor Exchanges

ABO blood type incompatibility or T cell crossmatch reactivity has generally precluded successful kidney transplantation. A crossmatch performed between the prospective donor and recipient may detect antibodies that would result in an accelerated rejection of the allograft. Natural antibodies to the A or B blood types can also cause immediate allograft loss. These biologic realities have circumvented the intent of a willing kidney donor to provide for needy recipient, until now (50). Recently however, protocols have been developed to overcome these barriers by using plasma exchange to remove either the isoagglutinin or HLA antibodies (see below) (51). Nevertheless, these "conditioning" regimens are still associated with an unpredictable rate of biological graft loss that could be averted by other innovative methods of live donor transplantation. One such approach is live donor exchange (i.e., exchanging donors incompatible with their intended recipients so that, instead, each donates to a compatible recipient). With donor exchange, the hazard of either blood type or crossmatch incompatibility can be avoided, while both recipients still derive the benefit of a living donor kidney transplant.

Section 301 of the U.S. National Organ Transplant Act of 1984 (NOTA), 42 U.S.C. 274e states: "It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation". Valuable consideration under NOTA § 301 has traditionally been considered to be monetary transfer or a transfer of valuable property between donor, recipient, and/or organ broker in a sale transaction.

However, in some regions of the world, the live donor exchange is considered to be valuable consideration; thus, it is not permitted. For example, Jeremy Chapman brought to attention a law in Australia that prohibits such exchanges that have occurred in the United States or Korea (52, 53). These exchanges are considered illegal in Australia because the donor is deemed to receive valuable consideration in return for the donation; therefore, it is not considered to be an altruistic donation. Carl Cardella presented a different interpretation to suggest that receiving a transplanted kidney is not the same as getting a monetary value; and that although it is obviously of value, it is not the same as buying and selling organs.

### The Gender Imbalance

Data were presented by Gil Thiel, Mahendra Bhandari, S. Adibul Hasan Rizvi, and Bob Metzger to reveal the following international experience: approximately 65% of live kidney donors have been women and approximately 65% of recipients have been men.

Abdullah Alkhader Al Sayari observed that among some living kidney transplants, there might be an unethical component of coercion and family/social pressures to bear. Participants agreed that these gender data display an excessive disparity, perhaps reflecting a psychological submission of women or discrimination of woman in many countries, including Western nations. However, there are more males than females with end stage renal disease, which may partly explain why there are more wives than husbands who donate in the case of transplants between spouses (54, 55).

S. Adibul Hasan Rizvi noted a Nobel laureate perspective to say, "the burden of hardship often falls disproportionately

on women." In some parts of the world, female gender bias is historically deep rooted. When the live related renal transplantation program was begun at the Sindh Institute of Urology and Transplantation, the factor of coercion was anticipated. In the prevailing culture, it was highly probable that females would have no choice but to donate a kidney. Dr. Rizvi reported that this donor coercion was encountered in the initial period, but it was subsequently overcome by efforts of a dedicated transplant team. Presently, despite existing cultural barriers, the female to male donor ratio at the Sindh Institute of Urology and Transplantation is 0.9:1.

Mahendra Bhandari endorsed the objective of establishing a genuineness of voluntary donation. In India, however, the family elder's domination is a reality of that culture; it is rare to find a prospective donor bold enough to decline. The issue is extremely sensitive and relevant in the case of female spouses as prospective donors.

Sadek Beloucif observed that accepting to donate depends on a number of contradictory considerations: the wish to help a member of one's family, with the family's opinion in the background, and the anticipation of possible loss of body integrity. The role of the doctor, who is the mandatory intermediary in the situation of donor consent, cannot be overlooked.

### Data and Perspective Regarding Minors as Donors

A review of the U.S. experience was presented by Bill Harmon. Minor donor kidneys were transplanted more frequently to adults than to pediatric recipients. Only 12% of the recipients from minor donors were identical twins (56). In some instances, minors gave their kidney to grandparents.

The use of a minor donor provided no better outcome than that expected from an adult donor. With the excellent outcome of unrelated transplantation from an adult living donor currently achieved, Forum participants agreed with the consensus proposal by Eduardo Santiago-Delpín that minors less than 18 years of age should not be used as living kidney donors.

### Risk Estimation for Donor Candidates with Medical Abnormalities

R. Steiner suggested that the ethical position of transplant centers could be best validated if kidney donor candidates were presented a defensible and quantitative estimate of medical risk. This risk assessment applies not only to "normal" donors but also to donors with isolated medical abnormalities (IMAs) such as hematuria, low grade proteinuria, hypertension, stone disease, and borderline normal GFR (57). Centers may accept some IMA donors considering the small risk of ESRD developing as result of the IMA (18). However, donors may reasonably ask whether their IMA entails an ESRD risk of 1 in 10, 1 in 100, or 1 in 1,000.

Steiner proposed that the risk of ESRD for many IMAs can be estimated semiquantitatively by knowing the prevalence of the IMA in the general population, and the incidence of the kind of ESRD with which that IMA might be associated. For example, suppose an IMA is present in millions of people in a population, but only one person a year in that population develops ESRD from that IMA. The risk is therefore much less

than for an IMA, present in 100 people in a population, that generates 50 new cases of ESRD caused by that IMA each year.

In the year 2000, almost 20,000 new cases of hypertensive ESRD were reported in the United States (58). Hypertension is common in the U.S. population, afflicting perhaps 25% of the population (59). The U.S. population in 2000 was about 280 million; therefore, there were about 70 million hypertensive patients, who produced almost 20,000 cases of hypertensive ESRD that year. When these data are expressed to "normalize" the yearly incidence of hypertensive ESRD for the prevalence of hypertension in the same population, the fraction has the units "new cases of hypertensive ESRD per hypertensive year." This fraction is the raw yearly risk for hypertensive ESRD for that hypertensive population. The raw yearly risk for hypertension in the United States is therefore 20,000/70,000,000 or 1 case in 3500 patient years. The 20-year risk for ESRD is 20 times the yearly risk, or 20 in 3500 (1 in 175). Based upon these data, the lifetime risk of ESRD that is associated with their isolated mild to moderate hypertension is less than 1 in 100.

The estimate of any IMA risk (hematuria, etc.) can be determined by the formula developed by R. Steiner:

$\text{Yearly risk for risk factor A} = (\text{Yearly incidence of ESRD A}) / (\text{Prevalence of risk factor A})$

The risk over the next  $n$  years is  $n \times$  the yearly risk. The yearly risk for ESRD for "medical condition A" that is assumed to be the only cause of "ESRD A" (e.g., hypertension and hypertensive ESRD) is the yearly incidence of "ESRD A" in the general population divided by the prevalence of "condition A."

When this epidemiologic method is used to calculate the baseline lifetime risk for any form of ESRD in the general U.S. population, assuming a population of 275,000,000, a yearly incidence of ESRD of 85,000, and a 70-year life span, the calculated lifetime ESRD risk is strikingly close to the figure determined by more sophisticated methods (2% for whites and 7% for blacks) (60). However, the formula above estimates the baseline two-kidney risk for ESRD that is associated with a given IMA, irrespective of donation. Predicting the effect of uninephrectomy on the progression of postdonation ESRD is a separate problem that applies only to the small fraction of donors with IMAs who actually will develop renal disease. Predicting the effect of nephrectomy is also a problem for "normal" donors, as some "normal" donors will develop diabetic nephropathy or other forms of ESRD after donation later in life (58). Even though their risks for ESRD are often lower, "normal" donors also need to know their risks, for the same reasons that apply to donors with IMAs.

### Determining Equipoise in the Risk-Benefit Analysis

Thomas Gutmann suggested the following: "In developing international standards of care for the live kidney donor and standards of medical suitability, the risk-benefit ratio of any proposed living donor transplant should be determined not only by medical facts, but ultimately by personal value judgments. These judgments should generally be made by the one most affected by the outcome—i.e., the prospective donor him/herself. After appropriate information has been given to the patients, the question of whether it is 'worth it' and the risks [are] 'acceptable' to the particular donor can

only be based on the character and values of that person and their actual relationship with the intended recipient."

### Pre-, Peri-, and Postoperative Issues

#### Determination of Cardiovascular Risk

Stephen Munn presented the following information. The clinical predictors of an increased perioperative cardiovascular risk (for noncardiac surgery) by the American College of Cardiology/American Hospital Association standards fall into three categories: major, intermediate, and minor (61). All major predictors (unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease) are contraindications to live kidney donation. Most of the intermediate predictors (mild angina, previous myocardial infarction, compensated or prior heart failure, diabetes mellitus) are also contraindications to donation, although a history of a myocardial infarction many years prior to the possible donation may not be an absolute contraindication. Minor predictors (older age, abnormal electrocardiogram, rhythm other than sinus, low cardiac functional capacity, history of stroke, or uncontrolled hypertension) warrant individual consideration.

Most potential donors will need only an electrocardiogram prior to surgery. Few potential donors may need a stress test such as a dobutamine stress echocardiogram (perhaps some >60 years of age), because most individuals with a significant cardiac risk factor should have been excluded from donation.

#### Smoking Cessation

Mehmet Haberal and Frederic Oppenheimer presented the following information. Pneumonia is the most serious complication following noncardiac surgery. It ranks as the third most common postoperative infection, behind urinary tract and wound infections (62). Smokers have a higher risk of pulmonary and wound infections after surgery than nonsmokers (63). No current evidence exists to suggest that smoking increases morbidity or mortality of live kidney donors; however, observational evidence suggests a benefit to cessation before surgery (64). Cigarette smoking is associated with an increase in tracheobronchial secretions and a decrease in mucociliary clearance. In smokers, the respiratory epithelium is altered, and poor ciliary activity combined with the production of more viscous mucus leads smokers to be more reliant on the cough to clear secretions from their lungs.

Abstinence of smoking for only 12 hours can greatly reduce carboxyhemoglobin concentrations, improve oxygen content and availability, and reverse negative inotropic and arrhythmic effects (65, 66). Smokers' polycythemia and increased blood viscosity take a few days to reverse (67). If smoking is stopped, sputum production declines over a 6-week period (65).

#### Alcohol Abstinence

Mehmet Haberal and Frederic Oppenheimer presented the following information. An increase in postoperative morbidity is reported for alcohol abusers who drink at least five drinks (>60 g ethanol) a day (68). Specific studies are lacking, but the result from observational evidence in other clinical settings is that alcohol misuse should be included in the pre-

operative assessment of live donors and withdrawal is recommended for at least 1 month before the operation (69).

Despite the high risk of complications, it was the experience of some Forum participants that recommendations to stop smoking and alcohol before elective surgery are not often heeded. There is a need for clinical guidelines for smokers and alcohol abusers in living donors undergoing surgery that include up-to-date patient information and four weeks of abstinence before surgery.

#### Forum Statement on Smoking Cessation and Alcohol Abstinence

- Smoking cessation at least 4 weeks prior to donation is advised, based on recommendations for patients undergoing elective surgical procedures.
- Cessation of alcohol abuse defined by DSM-3: 60 g alcohol/day sustained  $\geq 6$  months should be avoided for a minimum of 4 weeks to decrease the known risk of post-operative morbidity.
- All potential donors should have a health-promoting dialogue with the anesthesiologist or another health professional, which focuses on alcohol and smoking cessation in the context of other risk factors.

#### Assessment of Pulmonary Issues

Abdias Hurtado presented the following information regarding the determination of pulmonary risk in donor surgery. A careful history and physical examination are the most important parts of assessing risk (70). Routine preoperative pulmonary function testing (PFT) is not likely warranted for potential live kidney donors unless there is an associated risk factor such as chronic lung disease. Preoperative PFTs can be reserved to these patients. There are no cut-off values in PFTs; however, increased risk of postoperative pulmonary complication is associated with  $FEV_1 < 70\%$  or  $FVC < 70\%$  of predicted, or a ratio of  $FEV_1/FVC < 65\%$  (71). Patients with chronic pulmonary disease, who are at risk of the development end-stage pulmonary disease, should not be candidates for living kidney donation. Patients with asthma who are well controlled, and with a peak flow measurement  $> 80\%$  predicted, can be considered on an individual basis for live kidney donation (71).

#### Venous Thromboembolism

Factor V-Leiden, a variant of the coagulation protein Factor V, is associated with venous thrombosis, especially in oral contraceptive users. Factor V-Leiden is the most common hereditary blood coagulation disorder, present in 3–8% of the healthy white population (72). Marwan Masri has detected Factor V-Leiden mutant genes in 2% of living donors. In Britain, 5% of the population carries one or more genes for Factor V Leiden (far more than the number of people who will actually suffer from thrombosis). However, the odds ratio of a venous thrombotic event is 11 times greater in women taking oral contraceptives who have the Factor V Leiden mutation than for those who do not (73). Dan Brennan has also identified such a high rate of Factor V-Leiden in the U.S. population, suggesting that oral contraceptives and hormone replacement therapy be withheld for 3 months prior to an elective surgery.

Jonas Wadström suggested that potential living kidney donors should be evaluated by a comprehensive coagulation profile to include PT, PTT, antithrombin 3, protein S, and protein C, Activated protein C (APC) resistance, as well as an PT-prothrombin mutation, cardiolipin antibodies, and lupus anticoagulants. APC resistance is due to an inherited disorder of the Factor V molecule (usually Factor V-Leiden) and is again associated with venous thromboembolism.

However, there was no consensus on this particular issue of screening for a coagulopathy. Mark Stegall recommended that a history of venous thromboembolism be ascertained prior to an in-depth coagulation workup. Unless the history reveals a medical concern that would necessitate a comprehensive coagulation profile, these tests were considered expensive and not likely to yield consequential information.

#### Vascular Imaging

Sunil Shroff suggested that a noninvasive method of imaging such as magnetic resonance imaging or spiral CT scan (rather than a conventional contrast angiogram) could now be recommended, as these approaches are associated with less morbidity for the donor.

#### Conclusions

This report of the Amsterdam Forum presents a comprehensive review of the international practice of live kidney donation. Forum participants emphasize concordantly that medical judgment regarding the suitability of the potential donor is derived from a reflection of published data and physician experience. This report is intended to provide a compilation of information upon which appropriate medical judgment can be applied in the medical evaluation of every potential live kidney donor.

#### ACKNOWLEDGMENTS

The Forum was convened by the Ethics Committee of The Transplantation Society, administered by the National Kidney Foundation of the United States, and sponsored by the following: Novartis Transplantation and Immunology; Fujisawa Healthcare, Inc.; Roche Pharmaceuticals; Genzyme Corporation; Wyeth Pharmaceuticals; the International Society of Nephrology, the National Kidney Foundation of Singapore; and The Transplantation Society. We are also appreciative of the participation of representatives from the World Health Organization. Finally, we express our appreciation to Jennifer Martin, Gigi Polotski, and Sue Levey of the National Kidney Foundation for their administrative support.

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## **Appendix 4: A Report of the Vancouver Forum on the Care of the Live Organ Donor – Lung, Liver, Pancreas and Intestine Data and Medical Guidelines**

Originally published in *Transplantation*, Volume 81, Number 10, May 27, 2006.  
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## Introduction to Vancouver Forum

The burden and opportunity for successful organ transplantation is now regularly placed on the willingness of a well human being to provide at least one of these organs for transplantation: a kidney, a lobe of a lung, a segment of the liver, or a portion of their pancreas or intestine. The widespread acceptance of live organ transplantation is clearly counter to what historically had been a medical dictum to do no harm. Thus, the Forums in Amsterdam and Vancouver were conceived and developed because of the emerging hazards for those who are medically well and called on to donate an organ.

The goal of these Forums is to present definitive and timely statements regarding the responsibility of the transplant community for the live organ donor. And yet, these

efforts are works in progress being made by a nucleus of transplantation professionals to promulgate an international standard of care. The ethics of a continuing practice of live organ transplantation demands an international recognition that prioritizes a sustained well-being of the donor and not the intended recipient. The person who gives consent to be a live organ donor should be competent, willing to donate free of coercion, medically and psychosocially suitable, fully informed of the risks and benefits as a donor, and fully informed of risks, benefits, and alternative treatment available to the recipient.

**Francis L. Delmonico**

*Chairman of the Transplantation Society Ethics Committee*

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ISSN 0041-1337/06/8110-1372  
DOI: 10.1097/01.tp.0000220320.11404.98

# A Report of the Vancouver Forum on the Care of the Live Organ Donor: Lung, Liver, Pancreas, and Intestine Data and Medical Guidelines

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**A**n international conference of transplant physicians, surgeons, and allied health professionals was held in Vancouver, Canada, on September 15 and 16, 2005 to address the care of the live lung, liver, pancreas, and intestine organ donor. The Vancouver Forum was convened under the auspices of the Ethics Committee of The Transplantation Society. Forum participants included over 100 leaders in organ transplantation, representing many countries from around the world, including participants from the following continents: Africa, Asia, Australia, Europe, North and South America.

The objective of the Vancouver Forum was to develop an international standard of care for the live lung, liver, pancreas and intestinal organ donor. This Vancouver Forum followed a conference convened in Amsterdam on the care of the live kidney donor (1, 2).

There were four organ specific work groups at the Vancouver Forum: lung, liver, pancreas and intestine. Each organ work group addressed the following topics in concert and reported their findings in a plenary presentation to all participants:

- The evaluation of the potential live donor
- Criteria of live donor medical suitability
- Operative events, donor morbidity and mortality
- Responsibility and duration of donor follow up.

The Vancouver Forum also provided an opportunity for the Ethics Committee of The Transplantation Society to address issues of informed consent, the responsibilities of the transplant team, live donor selection, autonomy and satisfaction, and procedural safeguards. An ethics statement of the Vancouver Forum pertaining to these issues will be published separately by the Ethics Committee of The Transplantation Society. The transplant community has a responsibility for the care of the live organ donor. The death of a live donor is a tragedy of immeasurable proportion that brings an ethical dimension distinct from the complications that might be experienced in a recipient.

## Report from the Thoracic Group

Live donor lung transplantation generally involves three simultaneous operations: two donor lobectomies and a

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Received 14 February 2006.

Accepted 21 February 2006.

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ISSN 0041-1337/06/8110-1373

DOI: 10.1097/01.tp.0000216825.56841.cd

recipient bilateral pneumonectomy and lobar implantation. The use of live donors is occurring in cases in which the potential recipient mortality is high while awaiting for lung allografts from a deceased donor. With increasing experience however, the practice may expand to include elective patients (3, 4).

## I. Donor Evaluation

The goals of donor selection are to identify donors with excellent health, adequate pulmonary reserve for lobar donation and a willingness to accept the risks of donation without coercion (5, 6). A preference is given for family members or unrelated individuals with emotional attachment to recipient and/or family. A preference is also given for a spouse or donor with "significant other" relationship to the potential recipient.

The necessity of two live lung donors for a single recipient also brings a consideration of both parents as donors for the potential recipient. An element of coercion can always exist between any potential donor and the recipient and/or the recipient's other siblings. "Stranger" or "Good Samaritan" donation remains controversial with caution required in the screening process to exclude active or uncontrolled psychiatric disorders or inappropriate motivation, and ensure the altruistic nature of the donation.

The donor evaluation is a multi-phased process that begins with the potential recipient and family providing the names of potential donors with basic health information and height, weight, age, relationship, and smoking history. A preliminary psychosocial evaluation of selected donors is performed to assess the desire to donate. This evaluation includes a determination of the donor motivation, pain tolerance, feelings regarding the possible death of the potential recipient (and the donor) and the ability of the potential donor to be separated from family responsibilities and career obligations. Consultation with appropriate authorities regarding postlobectomy employability and insurability (life, disability insurance) is required.

Prospective donors should be informed of the morbidity associated with lobectomy and the potential for mortality, as well as for potential negative recipient outcomes in regard to life expectancy and quality of life after transplantation.

## II. Criteria of Live Donor Medical Suitability

The following are the eligibility criteria for living lobar lung donation:

- Age 18–60 years and able to give informed consent
- No active tobacco smoking or a significant smoking history

- No active lung disease/previous ipsilateral thoracic surgery
- No identifiable risk for familial lung disease (i.e. familial forms of idiopathic lung disease or pulmonary artery hypertension)
- No cachexia ( $BMI < 18 \text{ kg/m}^2$ ) or obesity ( $BMI \geq 30 \text{ kg/m}^2$ )
- ABO blood type compatibility with recipient
- Donor lobe size compatible with recipient hemithorax
- Normal pulmonary function and arterial blood gas results
- No conditions that significantly increase the risk of general anesthesia, surgery, and postoperative recovery
- No psychosocial, ethical issues, or concerns about donor motivation
- Not pregnant
- No active malignancy
- No active significant infection (HIV, hepatitis, acute CMV)

### **III. Operative Events, Donor Morbidity and Mortality**

The standard operative live donor lung transplant procedure is for the recipient to undergo a bilateral pneumonectomy and for two live lung donors to provide the left lower lobe and the right lower lobe simultaneously to the recipient (7, 8). Approximately 550 live lung donors constitute 98% of the global experience. The mean age was  $38 \pm 10$  years (range 18–60 years). Sixty percent of the live lung donors have been male, 76% have been related to the recipient and 24% were unrelated. Of the related donors, 40% were parents, 29% siblings, and 15% uncle/aunt. The remainder were cousins 9%, 5% son/daughter, 1% nephew/niece, <1% grandparent, and 1% miscellaneous. Of the live donors that were unrelated to the recipients 74% were friends, 20% spouses, and 6% strangers.

To date there has been no reported peri-operative mortality of a lung donor. There have been life-threatening complications in 3 donors (0.5%) with an intra-operative ventricular fibrillation arrest (1) and two with a postoperative pulmonary artery thrombosis. The mean length of the initial hospitalization following the lung lobectomy has been 8.5 days (range 3–36). Approximately 4% of live lung donors have experienced an intraoperative complication that included ventricular fibrillation arrest (1), the necessity of a right middle lobe sacrifice 7 (1.3%), the necessity of a right middle lobe re-implantation 6 (1.1%), the necessity of a non-autologous transfusion PRBC's 5 (0.9%) and a permanent phrenic nerve injury (1). Approximately 5% (27) of donors experienced complications requiring surgical or bronchoscopic intervention. These complications included bleeding (6), bronchopleural fistula (5), pleural effusion (5), empyema (2) bronchial stricture (2), pericarditis requiring pericardiectomy (2), arrhythmias requiring ablation (2) and a chylothorax (1).

There were 14 (2.6%) live lung donors that were readmitted to the hospital because of a pneumothorax, an arrhythmia, empyema, pericarditis, dyspnea, pleural effusion, bronchial stricture, bronchopleural fistula, pneumonia, hemoptysis, and dehydration. The long term (> one year) do-

nor complaints of live lung donors include chronic incisional pain, dyspnea, pericarditis, and non-productive cough.

### **IV. Responsibility and Duration of Donor Follow Up**

A constant awareness of the risk to the living donors must be maintained with any live donor organ transplantation program, and comprehensive short term follow-up should be mandatory. The Vancouver Forum Lung Group recommended that long term follow-up be strongly encouraged and funded by government/insurance authorities.

While the outcomes are well known in the recipient population, long-term consequences of live donor lobectomy have proven difficult to ascertain. Factors impeding long term follow-up include expense, distance from the transplant center, willingness of donors to participate, work load to the transplant center, and a general assumption that they are healthy. Many donors live far away from the transplant center and are reluctant to return for follow-up evaluation. The death of the recipient further exacerbates this situation.

Whether all donors have returned to their activities of daily living without restrictions is unknown. Responsibility for the care of the donor if complications occur varied widely among the centers represented within the Lung Group based on institution, country, and insurance system. In addition to the normal postoperative surgical clinic visit, recommended follow-up by the transplant center or the medical system in general ranged from one visit sometime between 3 months to one year, to multiple visits starting as early as three months and continuing generally through 1 to 3 years. Recommended testing in the follow-up also varied and included pulmonary function testing, 6-minute walk, chest radiography, quality of life surveys, and psychiatric evaluation.

### **Report from the Liver Group**

A potential recipient should be determined to be a suitable candidate for liver transplantation prior to the assessment of the potential donor. A set of practice principles was developed for live donor liver transplantation (but these principles could also be considered appropriate for organ transplants from lung, pancreas and intestine donors).

### **Principles of Live Liver Donation**

Live liver donation should only be performed if the risk to the donor is justified by the expectation of an acceptable outcome in the recipient.

The patient and graft survival of a live donor transplant should approximate the expected outcome for a recipient with the same disease etiology undergoing a deceased donor transplant.

- The indications for live donor liver transplantation should be the same as those established for deceased donor transplantation with the exception of institutionally-approved protocol studies that consider live donor transplantation preferential to liver transplantation from a deceased donor.
- Live donor liver transplantation should offer an overall advantage to the recipient when compared to waiting for an acceptable deceased donor organ to become available for transplantation. The decision to proceed with a live

donor liver transplant should be made after a careful analysis of the recipient risk to benefit ratio as it relates to severity of liver failure, quality of life and expected wait list time for a deceased donor.

- The estimated risk of mortality and morbidity currently associated with live donor right hepatectomy is 0.4% and 35% respectively. Since the risk to the donor is considerable, programs performing live donor liver transplantation should institute procedures and protocols that insure that donor mortality and morbidity is minimized.
- Concerning a pediatric recipient of a live liver donor (mostly parental), the patient and graft survival should be superior to the outcome for a recipient of the same disease etiology undergoing a deceased donor transplant.

### **Special Disease Indications for Live Donor Transplantation**

Special disease entity considerations were addressed that have been considered controversial: hepatocellular carcinoma (HCC), hepatitis C virus infection (HCV), and fulminant hepatic failure (FHF).

#### **Hepatocellular Carcinoma**

HCC fulfilling the Milan criteria (classified as a single tumor less than 5 cm or 3 or fewer tumors, each no more than 3 cm) is an acceptable indication for live donor liver transplantation (9). Until further data are available on improved preoperative staging and long-term follow up, the contraindications for live donor liver transplantation in patients with tumors exceeding the Milan criteria should be the same as that for deceased donor transplantation.

#### **Hepatitis C Virus Infection**

HCV cirrhosis is an acceptable indication for live donor liver transplantation. Early transplantation for hepatitis C with either a live donor or deceased donor may not be beneficial because of the risk of disease recurrence and unpredictable outcome. Thus, the appropriate timing for transplantation in hepatitis C requires further investigation, even though a liver may be more readily available from a live liver donor.

#### **Fulminant Hepatic Failure**

FHF is an acceptable indication for emergency live donor liver transplantation. Centers performing live donor liver transplantation for FHF should have the capacity to expeditiously complete the donor evaluation and education process. The ability to perform a rapid evaluation of the potential donor including blood tests, electrocardiogram, chest x-ray, pulmonary function test, echocardiography, imaging studies of the liver, psychological assessment and evaluation by the ethical board in a 24 to 48 hr time period is considered optimal.

### **I. Donor Evaluation**

The donor evaluation should be accomplished in a staged protocol that includes an independent donor advocate and a separate assessment of the recipient as a suitable candidate for a partial liver graft. The content of the donor evaluation should include:

- Initial screening of potential donors
- Complete history and physical examination
- Body weight and height (to calculate BMI)
- Laboratory testing
- No psychosocial, ethical issues, or concerns about the motivations of the donor. No active or uncontrolled psychiatric disorder.
- Imaging studies
- Possible preoperative donor liver biopsy

A complete history and physical examination including body weight and height should be obtained to exclude comorbidities that would significantly increase the donor risk. Biochemical donor evaluation should include: routine blood tests, serologies, a comprehensive coagulation profile and etiologic markers of liver disease. The donor should be screened for relevant endemic diseases that may have a detrimental effect on the donor (and possibly the recipient), e.g. asymptomatic schistomiasis and brucellosis.

The psychosocial/psychiatric evaluation should be conducted by a mental health care professional such as a psychiatrist, psychologist or social worker.

Appropriate radiologic imaging should be obtained preoperatively to assess liver volume and vascular anatomy. Biliary anatomy may be assessed either preoperatively or intraoperatively based upon the judgment of the surgical team.

#### **Donor Liver Biopsy**

A routine preoperative donor liver biopsy remains controversial (10, 11). The use of the body mass index as a predictor of hepatic steatosis, and thus the need for a donor liver biopsy is not absolute. Accurate quantification of hepatic fat as a contraindication to donation may not be afforded by BMI and imaging studies alone.

The recommendation of the Vancouver Forum participants was to suggest that a donor liver biopsy be performed if blood specimen liver tests are abnormal and steatosis or other abnormalities are noted on imaging studies. A liver biopsy may be considered if the BMI  $>30$  or in potential donors genetically related to a potential recipient with autoimmune hepatitis, primary sclerosing cholangitis or primary biliary cirrhosis.

### **II. Criteria of Live Donor Medical Suitability**

The following are the eligibility criteria for live liver donation:

#### **• Age**

There is insufficient data to define the upper age limit for living liver donation. Based upon reported general surgery data and experimental regeneration data, a limit of 60 years has been considered appropriate. However, live donor liver transplantation has been performed successfully with donors aged  $>60$  years. Minimal age is determined by ability to give legal consent.

#### **• Relationship**

Dr. Christoph Broelsch reported that German transplantation law requires living donors to be first or second degree relatives of recipients or have close emotional ties with them. This condition and the absence of any financial interest

for donation are evaluated by an ethical board. The Ethics Board in Germany is completely independent of the hospital evaluation team. A similar process exists in France. In Hong Kong, Doctors ST Fan and CM Lo reported that an application must be submitted to the Human Organ Transplant Board by the potential donor if the donor is not genetically related to the recipient (i.e. friends, in-laws), is a spouse of <3 years, or if the donor is genetically related but without proof of official documents (i.e. birth certificate or marriage certificate) to establish that relationship.

For many of Vancouver participants a genetic identity alone is not an essential criterion of suitability (versus sharing an emotional relationship). Otherwise, the use of a non-directed donor likely unknown to the potential recipient (now common in live donor kidney transplantation) was reported to be an unusual circumstance of live liver donation.

### **Body Mass Index**

General surgical experience indicates that a high BMI ( $>30 \text{ kg/m}^2$ ) may increase the risk of surgical complications. However, a BMI of  $>30$  may not affect graft quality and it is not an absolute contraindication to live liver donation.

### **Imaging**

Volumetric imaging analysis may overestimate the actual liver volume by 10%. Donor safety requires a calculated remnant liver of at least 30% of the original liver volume with complete venous drainage. Vancouver Forum participants concluded that in the interest of recipient safety an estimated graft liver volume to recipient body weight ratio (GWBWR) of  $>0.8\%$  should be achieved.

### **ABO Blood Type**

Compatible ABO blood type is recommended; however, ABO incompatible blood type live donor transplants may be undertaken in special instances such as infants  $<1$  year of age without the presence of isoagglutinins, and in emergency situations where no deceased donor allograft is available.

### **Liver Biopsy Results that Preclude Donation**

Histological findings that should preclude living liver donation are:

- Portal or sinusoidal fibrosis
- Non alcoholic steatohepatitis (NASH)
- Steatosis  $>20\%$  (only for right liver)
- Portal inflammation and necrotic-inflammatory changes.

Dieting is recommended for donors with steatosis. A repeated liver biopsy should be obtained after weight reduction.

### **• Laboratory Blood Tests**

Blood tests results that confirm donor infection with HIV, HCV or HBV (HBsAg+) are a contraindication for living liver donation. Testing for serum HBV DNA is recommended in donors with detectable anti-HBc with or without anti-HBs. Laboratory testing for a preexisting hypercoagulable condition should be performed especially if the potential donor has a history of venous thrombosis.

## **III. Operative Events, Donor Morbidity and Mortality**

### **• Thromboembolism**

Thromboembolism prevention following live donor liver transplantation is strongly recommended. Further, the presence of any unexplained postoperative cardio-pulmonary symptoms requires a radiologic investigation to exclude pulmonary emboli.

### **• Autologous Blood**

Storage of autologous blood is utilized by several institutions in the setting of right lobe donation. Technical progress has resulted in very low donor blood loss.

### **Recorded Complications**

The following definition of a complication was developed by the Vancouver Forum liver work group for a live liver donor:

- The result of a procedure performed on the donor
- A deviation from the ideal course
- Induces changes in management of patients (diagnostic/therapeutic)
- Occurs during surgical performance or recovery from the procedure.

The incidence of complications associated with live liver donation varies widely since a uniform definition of what constitutes a complication has been lacking. The Vancouver Forum participants recommended the international use of the Clavien system to record and grade live donor complications by severity (Table 1) (12), as previously used to assess morbidity of donor (13) and recipient (14) liver transplantation patients. Recently, a revised version of this classification, using a similar therapy based system to grade com-

**TABLE 1.** Clavien classification of surgical complications adapted for live liver donors: grade

#### Definition of the complication

##### Grade 1: Non-Life-Threatenind Complications

Require interventions only at the bedside,  
postoperative bleeding of less than 4 units of packed  
red blood cells, never associated with prolongation of  
ICU or hospital stay longer than twice the median of  
the population in study.

##### Grade 2: No residual disability

2a: Require only use of medication or 4 or more units of  
packed red blood cells.

2b: Require therapeutic interventions, readmission to the  
hospital or ICU, or prolongation of regular ICU stay  
for more than 5 days.

2ca: Any potential donor who has an aborted surgery.  
Donor surgery does not result in transplantation.

##### Grade 3: Residual disability

3a: There is low risk of death that results in permanent  
but not progressive disability.

3b: There is lasting disability that is either difficult to  
control or has a significant risk of death or liver failure.

##### Grade 4: Liver failure or death

4a: Lead to liver transplantation.  
4b: Lead to donor death.

**TABLE 2.** Survey of liver donor complications

21%: ELTR	14%: Brown et al.	28%: Lo CM
Death	Death (0.2%)	Bile leakage
Need for rehospitalization	Rehospitalization (8.5%)	Hyperbilirubinemia
Bile stricture or leak	Bile stricture or leak (6%)	Intra-abdominal collection
Liver insufficiency	Nonautologous blood transfusion (4.9%)	Small bowel obstruction
Pulmonary embolism	Need for reoperation (4.5%)	Biliary stricture
Major infection	Major infection (1.1%)	Portal vein thrombosis
Vascular		Pulmonary embolism
Major infection		Intra abdominal bleeding
		Pancreatitis
		Bleeding duodenal ulcer
		Incisional hernia
		Renal failure
		Gastric perforation
		Wound infection
		Gastric outlet obst.
		Pleural effusion
		Pneumonia
		Pressure sore
		Perineal nerve palsy

plications, was proposed, which may also serve to evaluate the outcome of live donors (15).

A list of donor complications reported in the United States, European and Asian experiences is listed in Table 2 (16, 17). Right lobe liver donation is associated with an increased morbidity (ranging from 20–60%, overall approximately 35%) and more severe complications than that associated with left lobectomy or left lateral segmentectomy.

The overall incidence of complications in the recently reported NIH sponsored Adult-to-Adult Live Donor Liver Transplant (A2ALL) cohort study is provided in Table 3 (13). At the time of the Vancouver Forum, 1008 donor candidates have been evaluated, 402 went to operating room with the intent of being a live liver donor however only 385 donated. There were 606 not accepted for live donation based upon either donor or recipient reasons.

#### Estimated Worldwide Operative Donor Mortality

To date, approximately 6000–7000 live donor hepatic resections have been performed worldwide for the purpose of transplantation and the rate of catastrophic complications is estimated to be 0.4–0.6% (Table 4). There have been 14 live donor deaths, 2 donors have undergone liver transplantation secondary to operative complications from right lobe donation and 1 donor is in a persistent vegetative state after donation. Mortality approaches 0.5% for the right lobe donor in contrast to approximately 0.1% for left lobe donation.

#### IV. Responsibility and Duration of Donor Follow Up

Live donors should be followed postoperatively for at least 1 year after the hepatectomy. Thereafter, follow-up may be desired but may not be always feasible because the residence of the donor is remote to the transplant center. Donor health insurance may influence the feasibility of long-term follow up. The Vancouver Forum participants recommended that a registry of live donor complications be established and

that donor deaths be reported to that registry. In the United States, the Organ Procurement and Transplant Network (OPTN) that is run by the United Network for Organ Sharing (UNOS) has recently made a live donor death or the necessity of a liver transplant following a donor hepatic resection a reportable event to the OPTN (18).

Several centers offering live donor adult liver transplantation are investigating the impact of donation on the donor's health and quality of life. Results from a survey sent to all individuals undergoing live liver donation in Japan through 2003 was presented at the Vancouver Forum by the Japanese Liver Transplantation Society. Of the 2667 live liver donors, 62% completed the survey with only half of the donors reporting complete recovery by 4 months postoperatively. Another 45% of donors reported near complete recovery with 90% of those individuals back to work or school. Only 3% of donors considered their recovery to be poor. A significant number of donors (40%) expressed anxiety regarding their future health. This anxiety was independent of the extent of liver resection since left lateral segment donors were equally concerned when compared with right lobe donors. Overall recipient mortality in this cohort was 17%. Of the recipients that died, 87% of their donor's were lost to follow-up.

The participants of the Vancouver Forum agreed that the transplantation community must continue to monitor the health and long-term outcome of the live liver donor. Financial disincentives to donation and the donor's ability to obtain and maintain health and life insurance must continue to be examined. The participants also considered an outcome that penalizes living donors for the act of donation to be unacceptable.

#### Report from The Pancreas Group

Patients with type 1 diabetes who are appropriate candidates for pancreas transplantation may be simultaneously

**TABLE 3.** A list of complications recorded in the Adult-to-Adult Live Donor Liver Transplant (A2ALL) study

A. Intraoperative Injury
1. Bile duct
2. Hepatic artery
3. Portal vein
B. Biliary complications
1. Bile leak/biloma
2. Biliary stricture
C. Abdominal/GI
1. Intra-abdominal bleeding
2. GI bleeding
3. Localized intra-abdominal abscess
4. Ileus (delayed return of bowel function for >7 days)
5. Bowel obstruction
6. Re-exploration
D. Cardiopulmonary
1. Myocardial infarction
2. Congestive heart failure
3. Pneumothorax (requiring chest tube)
4. Pleural effusion (requiring thoracocentesis)
5. Pulmonary edema
6. Cardiopulmonary arrest
7. Respiratory arrest
8. Aspiration
9. Pulmonary embolism
E. Wound Complications
1. Dehiscence
2. Hernia development
F. Liver-specific events
1. Encephalopathy
2. Ascites
3. Liver failure
4. Hepatic artery thrombosis
5. Portal vein thrombosis
6. IVC thrombosis
7. Transplantation
G. General
1. DVT
2. Neuropraxia
3. Infections
4. Psychological: depression, suicide, other

evaluated for suitable living segmental pancreas donors. Potential donors may undergo either segmental pancreas donation alone (for nonuremic or posturemic recipients) or simultaneous segmental pancreas and unilateral kidney donation (for uremic recipients). Once identified, potential donors will be subject to a thorough medical, metabolic and psychosocial screening. ABO and HLA cross-match compatibility is preferred but not mandatory. A segmental donor pancreatectomy can also be applied for islet isolation and allotransplantation (19, 20).

### I. Donor Evaluation

An initial screen will exclude donor candidates with a history of diabetes (including gestational), pancreatic disease, active or chronic infectious or malignant diseases. If a cross-match between the potential donor and recipient is negative, then a psychosocial evaluation would follow in the form of a screening interview by a social worker, with follow-up consultation with a staff psychiatrist/psychologist if deemed nec-

**TABLE 4.** Estimated worldwide operative donor mortality

• 6000–7000 live donor hepatic resections	11 right liver
• Two donors have undergone liver transplantation secondary to operative complications from right lobe donation	
• One donor is in a persistent vegetative state after donation	
• Catastrophic complications (0.4–0.6%):	
• 14 deaths	US 1
• 2 required liver transplant	Brazil 1
• 1 vegetative state	Germany 1
<b>3 left liver</b>	
	US 2
	Brazil 2
	Germany 2
	France 1
	Japan 1
	Egypt 1
	China (HK) 1
	India 1

For the right liver donor, the mortality is up to 0.5%.

For the left liver donor, the mortality is 0.1%.

essary. Caution is required in the screening process to exclude active or uncontrolled psychiatric disorders, and ensure the altruistic nature of the donation. Endocrinology consultation is done by a designated staff endocrinologist and a surgical consult by a designated donor surgeon.

Preoperative medical screening includes a detailed history and physical exam and the following laboratory investigations: complete blood count, serum electrolytes, blood coagulation profile, liver function tests, amylase, lipase, uric acid, hepatitis B and C profile, HIV testing, RPR, CMV IgG, EBV IgG, urine analysis; and a 12 lead EKG. Radiologic donor work-up includes chest x-ray and abdominal ultrasound, and after passing the metabolic and immunological tests (see below), an MRA/CTA to assess the anatomy of the pancreas and its vascular supply (19).

Additional tests specific for the live pancreas donor include preoperative metabolic screening of the live donor via the following:

1. Fasting glucose level (post 10- to 16-hr fast)
2. Hemoglobin A1c level

### 3. Oral glucose tolerance test (OGTT)

A >150 g carbohydrate diet is given for 3 days prior to the test and usual physical activity. After a 10 to 16 hr fast (water is permitted, smoking is not), a 75 g oral glucose load in 250–300 cc of water is given over 10 min. The end of the drink is time zero. Measurement of glucose and insulin is performed at the following intervals: -10, -5, 0, 15, 30, 60, 90, 120, 150, 180, 240 and 300 min.

### 4. Intravenous glucose tolerance test (IVGTT)

A >150 g carbohydrate diet is given for 3 days prior to the test and usual physical activity. After a 10 to 16 hr fasting period (water is permitted, smoking is not), the test is commenced between 0730 and 1000 hr.

A 0.5 g/kg dose (max. 35 g) of glucose is given IV over 3 minutes and 15 seconds. The end of the infusion is time zero. Glucose, insulin, glucagon and C-peptide are measured at the following intervals: -10, -5, 0, 1, 3, 4, 5, 10, 15, 20, 25 and 30 min.

Acute Insulin Response (AIR) to glucose is defined as the mean of the 3, 4 and 5 min insulin values following the glucose injection with the basal value subtracted. Glucose disposal rate (Kg) is defined as the slope of the natural log of glucose values between 10 and 30 min. after injection. First phase insulin release (FPIR) is defined as sum of insulin levels at 1 and 3 min.

## **5. Arginine stimulation test (AST)**

At the 35 min mark of the above test, 5 g of arginine (arginine HCl 10%) IV push is given over 30 seconds. Zero time is at the end of the bolus. Measurement of glucose, insulin, glucagon and C-peptide is performed at the following intervals: 0, 2, 3, 4, 5, 7, 10, 25 and 30 min. Acute insulin response (AIR) to arginine is defined as the mean of the peak three insulin values between 2 and 5 min following the arginine injection with the basal value subtracted.

## **6. Glucose potentiation of arginine-induced insulin secretion (GPAIS)**

About 60 min after the last blood draw in the above test, a glucose infusion (D20W) at 900 mg/min is started through an IV pump. The infusion is maintained for 70 min. At minute 60, 5 g of arginine (10% arginine HCL) IV is given over 30 seconds. The end of the bolus is time zero.

Measurement of glucose, insulin, glucagon and C-peptide is performed at the following intervals: 2, 3, 4, 5, 7 and 10 min. Acute insulin response at 900 mg/min glucose potentiation (AIR-900) is defined as the mean of the three peak insulin values between 2 and 5 min. with the basal value subtracted.

## **7. Insulin auto-antibodies (IAA)**

Measured by fluid phase radio-assay incorporating competition with cold insulin and precipitation with polyethylene glycol.

## **8. GAD 65 auto-antibodies (GAA)**

Measured in triplicate by radio-assay, using in vitro transcribed and translated recombinant human GAD (65-kDa isoform) and precipitation with protein A-sepharose.

## **9. Islet cell antigen 512 auto-antibodies (ICA512)**

ICA512 is measured by radio-immunoassay in duplicate using a 96-well plate format using a recombinant ICA512 protein.

Based on the history and physical exam in combination with the screening tests the following criteria will have to be met, in order to be considered a potential live segmental pancreas donor.

## **II. Criteria of Live Donor Medical Suitability**

### **General Inclusion Criteria**

Male and female segmental pancreas donor volunteers should be between the ages of 18 and 60. However, some

parental donors greater than 60 years of age would be acceptable in Japan. The difference regarding the age criterion in Asian countries may be necessitated because of the current lack of deceased donor alternatives.

The potential donor should be capable to provide written, informed consent; be mentally competent and be able to comply with the procedures and postoperative follow-up. Donor participation must be voluntary, without coercion and without financial incentives. The donor must also understand the nature of the procedure and the risks to his or her health. He/she must also be aware of the risks of recurrent disease in the donated graft.

### **Exclusion Criteria**

Subjects meeting any of the following criteria should be excluded as a segmental pancreas donor:

- Age >60 Years
- First-degree relative (parents/siblings/children) with type 1 or type diabetes (other than the potential recipient).
- Less than 10 years discordant from the recipient's age at the time of onset of diabetes. Example: If recipient is diagnosed as diabetic at age 22, donor must be at least 32 years old.
- Patients with active or uncontrolled psychiatric disorders
- Body mass index >28 Kg/m<sup>2</sup>.
- History of heavy smoking, obesity, hypertension, cardiac disease, cancer, gestational diabetes, alcoholism or excessive alcohol use, pancreatitis or peptic ulcer disease.
- Impaired glucose tolerance or diabetes by national diabetes group criteria
- Fasting blood glucose >110 mg/dl.
- HbA1c >6.0%.
- Any OGTT glucose levels >150 mg/dl.
- A glucose value >150 mg/dl during 75 g OGTT;
- 2-hour OGTT glucose >140 mg/dl (86).
- Glucose disposal rate <1% during IVGTT;
- Acute insulin response to glucose or arginine <300% basal insulin;
- Basal fasting insulin values >20 μU/ml;
- Elevated titer of islet cell antibodies;
- Clinical Evidence of insulin resistance;
- Evidence of >1 autoimmune endocrine disorder.

## **III. Operative Events, Donor Morbidity and Mortality**

Donor segmental pancreatectomy (tail) can be done open or laparoscopically. With increasing experience, however, the laparoscopic approach may actually have shorter operative times, as less dissection is required compared to the open technique (21).

### **Intraoperative and Postoperative Donor Complications**

#### **• Splenectomy**

A splenectomy may have to be performed in up to 15% of donors in case of insufficient collateral blood supply or bleeding. For that reason, all donors receive polyvalent pneu-

mococcal vaccine, hemophilus B and meningococcal vaccines 2 weeks prior to surgery.

#### ● Pancreatitis and pancreatic cyst(s), abscess or fistula

The incidence of such complications is less than 5%.

#### ● General postoperative complications

These include bleeding (with need for relaparotomy), prolonged ileus, pneumonia, DVT, wound infections, incisional hernia and others. The incidence of major general postoperative complications is less than 5%.

#### ● Esophageal/gastric varices

A rare, late complication is the development of upper intestinal bleeding secondary to esophageal/gastric varices (without portal hypertension) from venous collateralization in patients in whom the spleen was left in. A splenectomy is then required and is curative.

#### ● Risk of developing diabetes

If all criteria as assessed by the metabolic tests are met, the risk of the donor developing diabetes is less than 3% (22).

### **World Experience in Live Donor Segmental Pancreas Donation**

At the University of Minnesota, there have been 130 live donor pancreas transplants performed between 1977 and 2005. The distribution of these transplants was as follows: 40% pancreas transplant alone (PTA); 25% pancreas after kidney (PAK), and 35% simultaneous live donor pancreas and kidney transplants (SPK). There are 20 PTA and PAK live donor grafts functioning between 10 and 20 years following transplantation.

There are 3 living donor SPK transplants with function greater than 10 years.

At the University of Illinois, Chicago, 9 living-donor simultaneous kidney and segmental pancreas bladder-drained transplants were performed between 1997 and 2004 (23). Eight out of nine pancreas grafts and all the kidney grafts have been working for one to eight years following transplantation. There was no report of a donor death.

There have been 5 live donor segmental pancreatectomies performed in Japan, (4 in Chiba and 1 in Osaka), 1 case of live donor islet cell transplantation in Kyoto and 2 live donor segmental pancreatectomies performed in Seoul, Korea. At the University of Minnesota, there had been 2 live donor islet transplants after kidney transplantation early in the center experience (1970s).

### **IV. Responsibility and Duration of Donor Follow Up**

#### **Immediate Postdonation Follow Up**

The donor will have fasting and 2 hr postprandial blood sugar levels checked daily during hospitalization (19). The fasting and postprandial glucose levels should be determined monthly postdischarge. Blood glucose levels should be <110 mg/dl fasting and <140 mg/dl postprandial; above these levels will indicate the donor is in the diabetic range and in need of treatment. Glycosolated hemoglobin levels should be ob-

tained annually; above the normal range will also indicate development of diabetes and need for treatment.

The donor will generally have a postoperative hospitalization of about 5 to 7 days. Postoperative care of the donor is similar to that of any patient undergoing major abdominal surgery. A nasogastric tube is left in place until bowel function returns. Hemoglobin levels are checked serially as well as serum amylase, lipase, and glucose. Persistently elevated amylase and lipase may suggest pancreatitis, a leak, or pseudocyst formation. Persistent or severe left upper quadrant pain should be investigated with CT and a splenic radionuclide scan to assess the viability of the spleen. If the spleen appears infarcted, a splenectomy should be performed.

Donors are encouraged to maintain their body mass index of less than  $28 \text{ kg/m}^2$  with dietary counseling, if necessary (for certain ethnic groups the BMI should be even lower) (24).

The Vancouver Forum participants recommended the establishment of a pancreas donor registry and database for lifelong follow-up. Although no donor deaths have been reported after segmental pancreatectomy, a world registry should capture all cases performed.

#### **Report from the Intestinal Group**

Live donor intestinal transplantation has been the focus of two working groups organized to provide a technology assessment of this new surgical technique. The first consisted of surgeons and physicians experienced and interested in live donor intestinal transplantation who met in Brussels in July, 2005 at the 9th International Intestinal Transplant Symposium. The Vancouver Forum was the second meeting under the auspices of The Transplantation Society.

Intestinal transplantation is intended for the treatment of patients with life threatening complications of intestinal failure. The most common life threatening complication of intestinal failure is liver disease. Over the past five years the results of intestinal transplantation have improved dramatically, the result of a variety of factors including advances in immunosuppression, improved surgical techniques and evolving center experience (25).

Live donor intestinal transplants are not experimental but this procedure should be regarded as an innovative and an evolving technology. Because of the evolving nature of this procedure, the Vancouver Forum participants recommended that centers performing live donor intestinal transplantation should submit their protocols for ethical review and report outcomes to an international registry.

The lack of deceased donors and the resources otherwise needed for long term parenteral nutrition are the advantages afforded to a recipient of a live donor intestinal transplant. Combined liver/intestine grafts from live donors may have particular advantages in small infants who have a high mortality on the waiting list (26, 27). There are also immunologic advantages in the circumstance of identical twins (28). Whether HLA matching or reduced preservation times are truly beneficial is unproven and requires further study.

#### **I. Donor Evaluation**

Live intestinal donation should be voluntary without coercion. The potential donor should be in good health with

no underlying chronic medical illnesses that would increase the operative risk. There should be no history of intestinal surgery. Related donors (by HLA) must be excluded for potential recipients who have a genetic or familial intestinal disease. Caution is required in the screening process to exclude active or uncontrolled psychiatric disorders, and ensure the altruistic nature of the donation.

Donors are initially screened with an ABO blood type determination and in some instances with HLA as noted. Histocompatibility testing by T cell cross match should be negative. If there are multiple potential donors, ABO blood group identity and HLA matching may guide donor selection, especially in the circumstance of a presensitized candidate for whom a cross match negative donor might be identified.

Following completion of these initial steps, the testing that is done for the live donor evaluation is as follows:

- Physical examination and psychosocial assessment
- Gastroenterological assessment
  - D xylose and fecal fat absorption studies
  - Screen for celiac sprue
- Laboratory tests
  - CBC, PT/INR, PTT
  - Liver chemistries, amylase, renal chemistries, random glucose
  - Vitamin A, D, E, K, and B12
  - Ammonia, alpha fetoprotein, lipid profile
- Infectious disease assessment
- Hepatitis screen, HIV, CMV (IgM and IgG)
- EBV (IgM and IgG), VZV (IgA EIA)
- Urinalysis and culture; stool culture
- CXR and EKG
- Imaging studies
- Abdominal CT scan, 3D angio CT scan
- Superior mesenteric artery angiogram.

If no obstacles to successful donation are identified during the workup imaging studies are ordered. Imaging studies of the abdomen are performed to rule out any underlying or occult pathology and typically this is accomplished with a CT or ultrasound. To delineate the vascular anatomy CT or MR angiography is performed. If a traditional angiogram is performed patients must be informed of the risks.

## **II. Criteria of Live Donor Medical Suitability**

### **• Age**

There is insufficient data to define the upper age limit for living intestine donation. Based upon reported general surgery data a limit of 60 years has been considered appropriate. Minimal age is determined by ability to give legal consent.

### **• Relationship**

Living donors should be first or second degree relatives of recipients or should have close emotional ties with them. This condition and the absence of any financial interest for donation are evaluated by a physician team separate from the transplant program.

### **• Psychosocial Assessment**

There should be no psychosocial, ethical issues, or concerns about the motivations of the donor or active or uncontrolled psychiatric disorders.

### **• Body Mass Index**

General surgical experience indicates that a high BMI ( $>30 \text{ kg/m}^2$ ) may increase the risk of surgical complications. However, a BMI of  $>30$  may not affect graft quality and it is not an absolute contraindication to live donation.

### **• ABO Blood Type**

Compatible ABO blood type is recommended.

### **• Laboratory Blood Tests**

A comprehensive metabolic panel should be obtained. Blood tests results that confirm donor infection with HIV, HCV or HBV (HBsAg+) are a contraindication for living intestine donation.

## **III. Operative Events, Donor Morbidity, and Mortality**

The central caveat of the donor operation is to provide adequate length of intestine to the recipient to ensure enteral autonomy while preserving enough small bowel length in the donor. Some programs recommend small bowel decontamination the day prior to donation although there is little data to support this. The donor operation is performed through a midline incision. Most programs recommend the use of the live donor ileum (29, 30). Jejunal grafts have been also used but the procedure is more technically demanding (31). At the time of surgery the small bowel is mobilized and the vascular anatomy of the distal small bowel is examined. Blood flow to the remaining donor small bowel (in particular, the branch of the ileocolic artery feeding the ileocecal valve) must be preserved. With the use of either translumination of the mesentery and/or direct manipulation, the vasculature of the terminal superior mesenteric artery (SMA) branches is assessed. The distal branch of the SMA is identified, the mesentery is scored and the terminal branch of the SMA is dissected free from its take off of the ileocolic branch distally for about 2 centimeters. Alternatively the ileocolic artery can be used distal to the take-off of the right colic artery. The ileocolic artery may have advantages in the small donor (29). The segment of the superior mesenteric vein draining the graft is visualized next to the artery and is also dissected for approximately 2–3 centimeters.

The small bowel is measured. The standard procedure includes removal of approximately 150–200 centimeters of terminal ileum. It is essential to preserve at least two-thirds of the small bowel length in the donor. The distal 20–30 centimeters of donor ileum is preserved. The proximal distal end of the future allograft is stapled off, the blood vessels are

**TABLE 5.** Procedure-specific risk for the live intestinal donor

Short bowel syndrome
Small bowel obstruction
3 to 8%
3% mortality
Dysvitaminosis
Weight loss
Diarrhea

**TABLE 6.** List of the Vancouver Forum Participants

Abu-Elmagd	Kareem	University of Pittsburgh
Adcock	Lesley	Toronto General Hospital
Alabdulkareem	Abdulmajeed	Department of Hepatobiliary Sciences & Liver Transplantation
Aoe	Motoi	Okayama University
Barr	Mark L.	University of Southern California
Belghiti	Jacques	Hopital Beaujon, Paris University
Benedetti	Enrico	University of Illinois at Chicago
Berney	Thierry	Clinique do Chirurge Visceral
Bhandari	Mahendra	King George's Medical University
Bismuth	Henri	HepatoBiliary Center, Villejuif Cedex, France
Boggi	Ugo	Università di Pisa
Brand	Tracy	Canadian Council for Donation and Transplantation
Broelsch	Christoph	University Hospital of Essen
Brown, Jr.	Robert	Columbia University Medical Center
Capron	Alexander	World Health Organization
Chapchap	Paulo	Hospital Sirio Libanes and Hospital do Cancer
Cicalese	Luca	University of Massachusetts
Clavien	Pierre	Zentrum fur Klinische Forschung
Crawford	Michael	Liver Transplantation Unit, Royal Prince Alfred Hospital, Sydney, New South Wales
Cronin	David C.	Yale University
Dark	John	Freeman Hospital
Date	Hiroshi	Okayama University
Davis	R. Duane	Duke University Medical Center
Delmonico	Francis L.	Massachusetts General Hospital
Dew	Mary Amanda	University of Pittsburgh
Dib-Kuri	Arturo	The National Center of Transplants Mexico
Eghtesad	Bijan	The Cleveland Clinic Foundation
Emond	Jean C.	New York Presbyterian Hospital/Columbia
Fan	Sheung-Tat	University of Hong Kong Medical Center
Fazel	Iradj	Taleghani Hospital
Freise	Chris E.	University of California San Francisco
Friedewald	John	Northwestern Memorial Hospital
Fryer	Jonathan	Northwestern Medical Faculty Foundation
Fujimoto	Yasuhiro	Nagoya University Hospital
Garcia Valdecasas	Juan Carlos	Hospital Clinic, Barcelona, Spain
Ghobrial	Rafik Mark	The Dumont-UCLA Transplant Center
Ginns	Leo C.	Massachusetts General Hospital
Grant	David R.	The Toronto General Hospital
Greig	Paul	Toronto General Hospital/University of Toronto
Gruessner	Rainer	University of Minnesota
Gutmann	Thomas	University of Munich
Han	Duck-Jong	University of Ulsan
Hasegawa	Toshimichi	Osaka University Medical School
Hertl	Martin	Massachusetts General Hospital
Höckerstedt	Krister	Helsinki University Hospital
Humar	Abhinav	University of Minnesota
Hwang	Shin	Asian Medical Center, Korea
Ito	Toshinori	Osaka University Hospital
Jaffe	Bernard	Tulane University
Kamel	Refaat R.	Ain Shams University
Keown	Paul A.	Vancouver General Hospital
Keshavjee	Shaf	Toronto General Hospital
Khaghani	Asghar	Royal Brompton
Klintmalm	Goran	Baylor Regional Transplant Inst. Univ Medical Ctr.
Lake	John	University of Minnesota
Langnas	Alan N.	University of Nebraska Medical Center
LaPointe Rudow	Dianne	New York Presbyterian Hospital/Columbia
Lo	Chung Mau	The University of Hong Kong Medical Centre
Marcos	Amadeo	University of Pittsburgh Physicians
Margreiter	Raimund	University Hospital Innsbruck
Matas	Arthur	University of Minnesota
Matsumoto	Shinichi	Kyoto University Hospital
Mc Alister	Vivian	University of Western Ontario
McDiarmid	Sue	University of California, UCLA Medical Center

**TABLE 6.** Continued

McMurdo	Lisa	New York State Department of Health
Merion	Robert	University of Michigan Health System
Millis	J. Michael	University of Chicago Hospitals
Munn	Stephen	Auckland Hospital
Olthoff	Kim M.	University of Pennsylvania
Otte	Jean Bernard	Université Catholique de Louvain
Park	Soon J.	Physician Foundation @CPMC
Picciano	Fil	The Transplantation Society
Pomfret	Elizabeth	Tufts School of Medicine
Pruett	Timothy L.	Strickler Family
Rahmel	Axel	University of Leipzig
Reyes	Jorge D.	University of Washington
Rizvi	S. Adibul Hasan	Sindh Institute, University of Karachi
Schenkel	Felicia A.	University of Southern California
Squifflet	Jean-Paul	University of Liege
Strueber	Martin	Hannover Medical School
Sutherland	David E.	University of Minnesota
Tibell	Annika	Karolinska University Hospital
Todo	Saturo	University Hokkaido
Villamil	Fred	Fundacion Favaloro
Waddell	Thomas K.	Toronto General Hospital
Wahlin	Staffan	Karolinska University Hospital in Huddinge
Wain	John C.	Massachusetts General Hospital
Wiesner	Russell	Mayo Clinic Rochester
Wood	Kathryn	President, The Transplantation Society
Woodhouse	Michael	Genzyme, Inc.
Wright	Linda	University Health Network, University of Toronto.
Yusen	Roger D.	Washington University
Zuckermann	Andreas	University of Vienna

clamped, and the portion of segment of small bowel is removed to the back table where it is flushed with preservation solution. Most programs are using University of Wisconsin solution.

There was one report of using only 60 centimeters of distal jejunum and proximal ileum which did not achieve nutritional autonomy. Another approach consisted of using a donor graft consisting of the distal ileum and ileocecal valve with a portion of the cecum. In this case, the donor had evidence of protracted diarrhea and dysvitaminosis.

The procedure specific risk for the live intestinal donor is given in Table 5. The risk of perioperative death is probably similar to the risk of general anesthesia, approximately 0.03%. It could be anticipated that following a small bowel resection about 3 to 5% of donors will eventually develop a small bowel obstruction (30–38). In large series the mortality rate for patients with small bowel obstruction is about 2%. This risk will exist for the lifetime of the patient. Whether HLA matching or reduced preservation times are truly beneficial is unproven and requires further study. Table 6

#### IV. Responsibility and Duration of Donor Follow Up

The World experience with live intestine donation is limited. According to the intestinal transplant registry as of March 31, 2005, 65 transplant centers have performed 1,292 intestinal transplants. Identified within that database there were 61 transplants where a living donor was the source of the organ. This was performed in a total of 16 transplant centers

and there are currently 21 survivors of these living donor intestinal transplants. There were no donor deaths or long term morbid complications of intestinal donors reported at the Vancouver Forum.

The types of all intestine transplants performed to date include approximately 570 isolated small bowel transplants, 490 combined live and small bowel transplants, and 232 multi-visceral transplants. There are currently 658 survivors (25). Patient and graft survival was similar between live donor and deceased donor transplants. Nutritional autonomy and causes of graft failure and patient death were similar between both groups.

The center performing the donor procedure has a responsibility to ensure long term medical care of any procedure-related complication. The recommended minimum follow up schedule includes a postoperative visit at 2 and 4 weeks. There are several problems that can occur early in the postdonation period such as small bowel obstruction, diarrhea, weight loss and dysvitaminosis. Donors should be followed until all procedure-related symptoms have been resolved. The donor team needs to be wary of a B<sub>12</sub> deficiency. B<sub>12</sub> monitoring can be performed with serum levels at 6 months and annually for 3 years.

The long term risk of small bowel donation primarily involves of small bowel obstruction in the range of 1% to 5%. With the development of a complete small bowel obstruction there is approximately 1 to 2 % mortality rate.

The intestinal group made the following action plans and recommendations:

1. Creation of a donor registry in conjunction with the existing international intestinal transplant registry
2. Data collection to study effect of organ preservation time, and HLA matching results with next International Intestinal Transplant Registry Report
3. Collect and share with intestine transplant centers, the UNOS data on waiting list death /withdrawals for patients waiting for isolated intestine grafts

## CONCLUSIONS

The mission of the Vancouver Forum is to convey an international concern for the well being of the live organ donor and to promulgate a reference of care by an internationally renowned group of experts. The decision to proceed with live donor transplantation should be made only after a careful analysis of the recipient risk to benefit ratio as it relates to etiology of disease, quality of life, expected morbidity and mortality on the waiting list. This decision will also be influenced by the availability and quality of any potential deceased donor organ.

The Vancouver Forum participants acknowledge the heroism of those living volunteers who have provided a life saving organ for a transplant recipient. The Forum participants also recognize the societal contribution that live organ donors have made by reducing the waiting list for transplantation of organs from deceased donors.

## ACKNOWLEDGMENTS

*The Vancouver Forum was convened by the Ethics Committee of The Transplantation Society. We express our appreciation to Charlotte Berlin of Astellas Pharmaceuticals for the educational grant that enabled the Vancouver Forum to be convened. We also wish to thank Catherin Parker and Filomena Picciano of The Transplantation Society, Central Business Office, for their administrative support.*

*The authors also wish to acknowledge Abdulmajeed Al Abdulkareem, Pierre Clavien, Arturo Dib Kuri, Mark Ghobrial, Martin Hertl, Goran Klintmalm, CM Lo, Vivian McAlister, Raimund Margreiter, and Jean-Bernard Otte for their helpful comments in their review of the manuscript.*

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# The Ethics Statement of the Vancouver Forum on the Live Lung, Liver, Pancreas, and Intestine Donor

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The use of organs from live donors is an important component of transplantation today. The Ethics Committee of the Transplantation Society (TTS) has previously published a statement on ethical considerations pertaining to the live kidney donor (1). Evolving technologies have now allowed for the successful transplantation of organs from the live lung, liver, pancreas and intestine (extrarenal) donors. The Ethics Committee of TTS was convened at the Vancouver Forum to deliberate upon the use of live donors for extrarenal transplantation. The following is a summary of the committee's deliberations. We believe that live extrarenal donation should proceed within the context of the ethical principles established for live kidney donation. The physical and psychosocial welfare of a healthy donor must be put in context of the needs of the recipient and impact of the recipient's illness upon the donor. In principle, the Ethics Committee of TTS recommends that live lung, liver, pancreas and intestine donation should only be performed when the aggregate benefits to the donor-recipient pair (survival, quality of life, psychological, and social well being) outweigh the risks to the donor-recipient pair (death, medical, psychological, and social morbidities).

At the Vancouver Forum, emerging data pertaining to the aggregate risks and benefits of live lung, liver, pancreas and intestine transplantation provided more information regarding the factors that enter into the ethical decision to place a healthy person in harms way. It is now evident that live donors are the sole source of organs for transplantation in many societies; however the limited availability of information about outcomes for the donors and recipients mandates

that live lung, liver, pancreas and intestine organ donation and transplantation must proceed with thoughtful independent oversight and transparency. As organs recovered from deceased donors offer substantial (and sometimes superior) benefits to potential recipients, with no risk to a healthy, live donor, efforts to maximize the use of organs from deceased donors must not be impeded by the development of live organ donation.

This consensus statement comes from the deliberations of the Ethics Group of the Vancouver Forum which was charged with defining the essential ethical elements of the process for the transplant center performing live lung, liver, pancreas and intestine donor. Special emphasis upon elements and issues of informed consent, assurance of donor autonomy and the patient selection process is included for clarity.

## Responsibility of the Transplant Team Performing Live Donation

- Information about organ donation and transplantation should be provided repetitively to the prospective donor in order to facilitate the decision to proceed with live organ donation.
- Medical, psychological and social suitability should be determined after complete and thorough evaluation by a team that has the expertise to assess the suitability of an individual for organ donation.
- If medical conditions are identified in a prospective donor that need treatment (some may preclude donation), then the transplant team should counsel and encourage acquisition of medical care to treat such conditions.
- Recognizing that the donation process is stressful whether or not it proceeds, psychological support should be available throughout the evaluation and donation process.
- Live organ donation should be voluntary and the transplant team should make efforts to assure that the decision to donate is voluntary and has not been manipulated.
- Medical care for the donor should be provided until there is recovery from the donation procedure.
- Quality assurance/improvement procedures should be utilized to decrease risk during the donation process.
- The transplant center should facilitate the long-term follow-up and treatment of the donor with donation related acquired conditions.
- The transplant center should contribute to the general knowledge base by reporting complications and outcomes to registries and the medical community.
- The transplant center should work with appropriate authorities, agencies and insurance companies (as applicable) to minimize disincentives and penalties towards live organ donation.

A transplant center that performs live organ transplantation must implement procedural safeguards to enhance do-

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Received 30 January 2006.

Accepted 30 January 2006.

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ISSN 0041-1337/06/8110-1386

DOI: 10.1097/01.tp.0000214976.36526.e3

nor understanding, safety and autonomous decision-making. These are considered to be essential to the process of live organ donation, particularly for the live lung, liver, pancreas and intestine donor.

The essential procedural components include:

- Inclusion of health care professionals in the donation process, who are exclusively responsible to the donor's evaluation and welfare. Such an individual should not have direct contact with the recipient or be overtly influenced by concerns for the recipient.

• Repetition of the information pertaining to live donation, in recognition that informed consent is a process not an event.

- Psychosocial evaluation, to include the capacity of the donor to process information and give informed consent.

Additional safeguards may include:

- Reflection period after medical acceptance and decision to donate.
- Assessment of donor retention of information and understanding.
- External review committees.

### Informed Consent

Informed consent from an individual is essential in the performance of live organ donation. The prerequisites for an individual to give informed consent are that

- The potential donor must have a cognitive capacity sufficient to make the decision to donate.
- The decision must be voluntary.
- The donor must receive and understand relevant and sufficient information about the procedure.

Informed consent is predicated upon the individual's receipt of adequate information about the evaluation process to become an organ donor and the donation procedure and possible consequences. The disclosure should include information about the associated risks, including but not limited to:

- The risk of death, reported worldwide and at the center where the procedure is proposed.
- Medical morbidities.
- Changes in health and organ function.
- Impact upon insurability/employability.
- Potential effects on family and social life.
- Psychological impact of donation and nondonation.

In addition, the potential donor should be given information about:

- The responsibility of the individual and health and social systems in the management of discovered conditions (such as the discovery during the evaluation process of HIV, tuberculosis or other transmissible diseases);
- Any specific recipient conditions which may impact upon the decision to donate; however, no information can be given to the potential donor until permission is obtained from the recipient;
- Expected transplant outcomes (favorable and unfavorable) for the recipient.
- Information on alternative types of treatments for the recipient, including deceased organ transplantation;
- The limited information available on extrarenal live donation results in uncertainty about donor and recipient outcomes;

- The request that the potential donor participate in long-term information gathering (registries) to increase the knowledge base.

### Donor Autonomy

The decision to donate must be voluntary and the individual *must* be reassured that:

- The freedom to withdraw from the donation process at any time exists, without consequence and within a supportive environment;

- Medical and other reasons for not proceeding with donation will be kept confidential.

However,

- Donor consent and autonomy is necessary, but not sufficient to proceed to donation; medical evaluation and concurrence are essential;

- Donor autonomy does not overrule medical judgment and decision making.

### Donor Selection

Individuals who are legally incompetent or who lack the capacity for autonomous decision-making should not be donors. In the rare instance that these individuals might be considered as live organ donors, an independent advocate for the donor must be appointed using the mechanisms available within a particular society.

- In the event that non-directed or distant acquaintance live organ donation is entertained, special considerations to prevent donor exploitation should be made.

- Because many of the long-term consequences of extrarenal organ donation are not known, centers should consider long-term access to health care after the procedure as a prerequisite for donation.

- The donation process and follow-up should be cost neutral for the donor.

The use of healthy individuals to provide extrarenal organs for transplantation is predicated upon donor voluntariness and the aggregate benefit to the individuals outweighing the aggregate risk of adverse outcomes. Additional Ethics Committee recommendations are hampered by insufficient information pertaining to donor and recipient outcomes after live lung, liver, pancreas and intestine donation. As a consequence, procedural elements become paramount in the process in order to safeguard personal and system integrity, while minimizing the risk for exploitation of the donor. Voluntariness is predicated upon willingness to donate, with an understanding of the associated risks and benefits of the process. Without additional information relating to likely outcomes from extrarenal live donation, the informed consent process will be incomplete. There is a clear need for more information on short and long term consequences and risks associated with live donation of lung, liver, pancreas and intestinal organs. The transplantation community and the individual transplant team have a responsibility to collect and share data on donor outcomes in a consistent and comparable fashion. National, international and/or organizational donor registries should be established and maintained.

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1. The Consensus Statement of the Amsterdam Forum on the Care of the Live Kidney Donor. *Transplantation* 2004; 78(4): 491–492.

## Appendix 5: Forum Agenda

### Thursday, February 9, 2006

#### 17:00 **Forum Opening**

- Welcome – Dr. Penny Ballem, Deputy Minister, BC Ministry of Health
- *Opening Remarks* – Dr. David Hollomby, CCDT Council Member, Organ Transplantation Committee Chair
- *Forum Process* – Dorothy Strachan
- *Challenge Address* – Dr. Sandra Cockfield, Forum Co-Chair and Medical Director, Living Donor Program, U of A
- *Living Donation: Past, Present and Future* – Dr. Francis Delmonico, Professor of Surgery, Harvard Medical School and President of the Organ Procurement and Transplantation Network and the United Network for Organ Sharing

### Friday, February 10, 2006

#### 08:00 **Part I – Living Donation: Risks and Benefits**

##### a. Informing the Donor

- *Living Donor Experience* – Ken Donohue
- *Overview: Ethical Challenges* – Linda Wright, Bioethicist, University Health Network, Toronto
- *Balancing Risk and Patient Autonomy* – Dr. Robert Steiner, Professor, Clinical Medicine University of California, San Diego

#### 10:15 **Challenge Questions**

#### 12:00 **Forum Recommendations Group Mtg.**

#### 13:30 **Part I – Living Donation: Risks and Benefits (cont'd)**

##### b. Medical/Surgical Risks of Living Donation

##### Organ Specific Panel

- Dr. Amit Garg, Assistant Professor, Departments of Medicine and Epidemiology, University of Western Ontario (kidney)
- Dr. Paul Greig, Professor, Department of Surgery, University of Toronto (liver)
- Dr. John Mullen, Clinical Professor of Surgery, University of Alberta Hospital (lung)

#### 14:40 **Canadian Survey Results: Incremental Risk and Decision Making** – Dr. Diane Hébert, Forum Co-chair

#### 15:10 **Challenge Questions**

#### 16:45 **Closing**

#### 18:00 **Forum Recommendations Group Mtg**

## Saturday, February 11, 2006

08:00	<b>Report: Forum Recommendations Group</b>
08:45	<b>Part II – Psychosocial Considerations</b>
	<ul style="list-style-type: none"><li>• <i>Canadian Survey Results: Psychosocial Evaluation</i> – Dr. Sandra Cockfield</li><li>• <i>Psychosocial Aspects of Living Organ Donation</i> – Dr. Mary Amanda Dew, Professor of Psychiatry, Psychology and Epidemiology, University of Pittsburgh</li></ul>
10:00	<b>Challenge Questions</b>
11:20	<b>Part III – Long-Term Follow-up</b>
	<ul style="list-style-type: none"><li>• <i>Canadian Survey Results: Follow-up</i> – Dr. Diane Hébert</li></ul>
11:30	<b>Challenge Questions</b>
12:30	<b>Forum Recommendations Group Mtg.</b>
14:00	<b>Part IV – Consent: Legal and Ethical Challenges</b>
	<ul style="list-style-type: none"><li>• <i>Canadian Survey Results – Consent</i> – Dr. Diane Hébert</li><li>• <i>Legal and Ethical Considerations in Informed Consent</i> – Tim Caulfield, Professor of Law, Health Law Institute, University of Alberta</li><li>• <i>Donor and Family Decision Making</i> – Dr. Mary Amanda Dew</li></ul>
15:30	<b>Challenge Questions: Table discussions</b>
17:15	<b>Closing</b>
18:00	<b>Forum Recommendations Group Mtg.</b>

## Sunday February 12, 2006

08:00	<b>Report: Forum Recommendations Group</b>
09:00	<b>Part V – Perspectives: Economic Implications of Living Donation</b>
	<ul style="list-style-type: none"><li>• <i>Canadian Survey Results: Financial Barriers</i> – Dr. Sandra Cockfield</li><li>• <i>Health Economics</i> – Dr. Scott Klarenbach, Assistant Professor, Department of Medicine, University of Alberta</li><li>• <i>Models for Reimbursement</i> – Dr. Scott Klarenbach</li><li>• <i>Insurance Considerations</i> – Dr. Robert Yang, Nephrologist, London Health Sciences Centre</li><li>• <i>Legal Issues</i> – Tim Caulfield</li></ul>
10:50	<b>Challenge Questions</b>
12:20	<b>Plenary Wrap-up</b>
13:00	<b>Forum Closing</b>
13:00	<b>Forum Recommendations Group Mtg.</b>
15:30	<b>Forum Recommendations Group Closing</b>

## **Appendix 6: Participants**

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## **Appendix 7: Forum Background Documents**

The following documents can be downloaded from the CCDT website at [www.ccdt.ca](http://www.ccdt.ca):

1. Steering Committee, Enhancing Living Donation: A Canadian Forum (2006). *Enhancing Living Donation: A Canadian Forum—Report and Recommendations*. Edmonton: The Canadian Council for Donation and Transplantation.
2. Caulfield, Timothy. *Living Organ Donation: Consent Challenges*. Edmonton: The Canadian Council for Donation and Transplantation.
3. Cockfield, Sandra M. *Environmental Scan of Living Organ Donor Programs in Canada*. Edmonton: The Canadian Council for Donation and Transplantation.
4. Dew, Mary Amanda; Switzer, Galen E.; DiMartini, Andrea F.; Myaskovsky, Larissa; Crwoley-Matoka, Megan. *Psychosocial Aspects of Living Organ Donation*. Edmonton: The Canadian Council for Donation and Transplantation.
5. Garg, A.; Knoll, Greg.; Muirhead, Norman and Prasad, Ramesh. *Medical Risks of Becoming a Living Kidney Donor—What is known and what needs to be known*. Edmonton: The Canadian Council for Donation and Transplantation.
6. Klarenbach, Scott; Vlaicu, Sorina; Garg, Amit; Yang, Robert; Clark, Katie; Dempster, Todd. *A Review of the Economic Implications of Living Organ Donor Donation: Donor Perspectives and Policy Considerations*. Edmonton: The Canadian Council for Donation and Transplantation.
7. Lien, Dale and Mullen, John. *The Risks of Living Lung Donation*. Edmonton: The Canadian Council for Donation and Transplantation.
8. Wall, William. *Living Donor Liver Transplantation Overview*. Edmonton: The Canadian Council for Donation and Transplantation.

## **Appendix 8: CCDT Fora and Reports**

The following reports from CCDT fora are posted on the CCDT website ([www.ccdt.ca](http://www.ccdt.ca)):

### **Severe Brain Injury to Neurological Determination of Death (April 2003)**

The report is endorsed by the CCDT, Canadian Critical Care Society, Conference of Chief Coroners and Medical Examiners of Canada, Canadian Association of Emergency Physicians, Canadian Neurological Society, Canadian Neurosurgical Society, Canadian Neurocritical Care Group, Canadian Association of Transplantation, Canadian Society of Transplantation, Québec-Transplant, Trillium Gift of Life Network and its ICU Advisory Group, Alberta Health and Wellness, British Columbia Transplant Society.

### **Medical Management to Optimize Donor Organ Potential (February 2004)**

The report is endorsed by the CCDT, Canadian Critical Care Society, Canadian Association of Transplantation, and Canadian Society of Transplantation. Guidelines were published (CMAJ, CJA).

### **Assessment and Management of Immunologic Risk in Transplantation (January 2005)**

Clinical and laboratory specialists from transplant programs across Canada convened to examine current practices, literature and new technologies for the assessment of human leukocyte antibodies pre-transplant with the goal of being able to develop recommendations on best practices. Consensus recommendations will be used to improve immunologic risk assessment and management in transplantation with the goals to improve solid organ transplant outcomes; improve equity of access to organ transplants for highly sensitized patients; reduce the wait-list time for highly sensitized patients; and increase the number of organ donors.

### **Donation after Cardiocirculatory Death (February 2005)**

Post-forum public survey shows substantial support for proceeding with this type of donation in Canada. Guidelines were published (CMAJ).