United Kingdom Guidelines for Living Donor Kidney Transplantation

Paulette Cain, who donated a kidney to her husband, David.

"People say it was a generous thing to do. However, in reality, I wanted it for myself and Jade, our young daughter, as much as for David because the strain on our lives was so great."

Tom Bortey (right), who received a kidney from his brother George.

"If my brother hadn't donated his kidney there would have been no hope for me. I owe it to other black people to tell them our story, so they can think about making a donation."

Chris Kemp, who gave a kidney to his son, Oliver.

"Having only one kidney certainly doesn't stop me doing things. Oliver and I joke about the transplant sometimes. I tell him he's had my money – he might as well have my body!"

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UNITED KINGDOM GUIDELINES FOR LIVING DONOR KIDNEY TRANSPLANTATION

COMPILED BY A JOINT WORKING PARTY OF THE BRITISH TRANSPLANTATION SOCIETY AND THE RENAL ASSOCIATION

SECOND EDITION APRIL 2005

THIS SECOND EDITION OF THE GUIDELINES BUILDS UPON THE WORK OF THE FIRST. WE ARE ONCE AGAIN INDEBTED TO NUMEROUS COLLEAGUES WHO ASSISTED THE WORKING PARTY IN THE PREPARATION OF THIS DOCUMENT BY CONTRIBUTING THEIR EXPERTISE AND ADVICE.

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CONTENTS

12.0 THE HIGH RISK RECIPIENT

12.1 The highly sensitised recipient: desensitisation and ABO blood group incompatible living donor kidney transplantation (to be augmented when future UK Guidelines are developed)

13.0 RECURRENT RENAL DISEASE

13.1 Primary hyperoxaluria
13.2 IgA nephropathy
13.3 Membranous glomerulonephritis
13.4 Diabetes mellitus
13.5 Cystinosis
13.6 Amyloidosis
13.7 Focal segmental glomerulosclerosis
13.8 Alport's, crescentic glomerulonephritis, vasculitis
13.9 Haemolytic uraemic syndrome
13.10 Systemic lupus erythematosus
13.11 Mesangiocapillary glomerulonephritis

14.0 LIVING DONOR KIDNEY TRANSPLANTATION IN CHILDREN

1.0 INTRODUCTION AND BACKGROUND

1.1 THE NEED FOR GUIDELINES

The setting of standards and the provision of clinical guidelines describing best practice are fundamental in all areas of clinical medicine. In 1998 the British Transplantation Society (BTS) recognised the need to set standards in clinical transplantation and published "Towards Standards for Organ and Tissue Transplantation in the United Kingdom" (1), which was subsequently updated in 2003 (2). Although the 1998 version included aspects of living donor transplantation, a more comprehensive and focused document was published in 2000, "United Kingdom Guidelines for Living Donor Kidney Transplantation", in collaboration with the Renal Association (RA) (3).

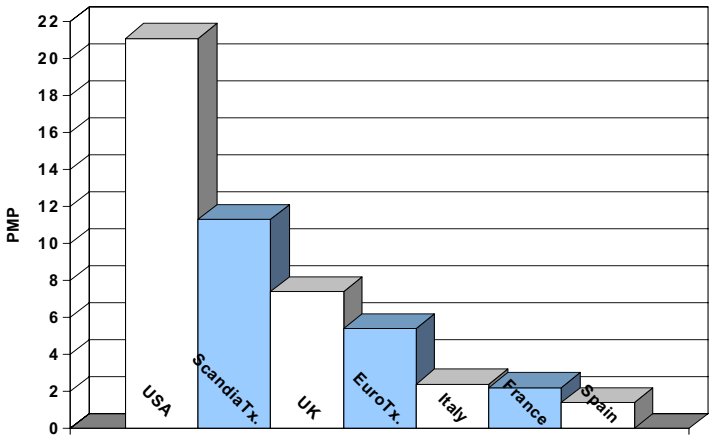
Living donor kidney transplantation provides patients with end-stage renal disease (ESRD) with the best chance of long-term rehabilitation. The opportunity for planned transplantation before dialysis becomes inevitable is an attractive option for patients and evidence suggests that there is improved graft survival in transplants performed pre-emptively, making it the treatment of choice (4). The use of kidneys from living donors offers the best opportunity to achieve this and so maximise benefit to patients.

During the last 5 years there has been substantial growth in living donor kidney transplantation in the UK but there is still considerable room for expansion in comparison with activity in Scandinavia and the United States of America (USA). (Table 1.1.)

The increase in UK activity can be attributed to a number of factors including improved patient awareness, innovative surgical techniques with minimally invasive/laparoscopic nephrectomy surgery to minimise donor morbidity and acceptance that outcomes from living genetically unrelated donors are equal to traditional genetically related donations.

In addition, there has been increased funding for living donor programmes from the Department of Health via UK Transplant, which has facilitated the appointment of dedicated living donor co-ordinators in transplant centres nationwide.

Table 1.1.
Living Donor Kidney Transplantation Activity 2003



Data from UKT and UNOS

Despite initiatives to increase donation from deceased donors through non-heart beating and donor liaison schemes, the broadening of criteria to include 'marginal' deceased donors and by encouraging more people to join the Organ Donor Register, there is still a donor organ shortfall. Kidneys from living donors now make a significant contribution to increasing the number of organs available for transplantation; the latest evidence shows that in the UK one in four kidney transplants is now performed from a living donor (5).

The main objections to living donor kidney transplantation are associated with the welfare of the donor; both through exposure to major surgery, which is not required for the purposes of improving the health of the donor, and the long-term concerns of life with a solitary kidney. A realistic appraisal of the risks must be presented to the donor based upon the best evidence.

1.0 INTRODUCTION AND BACKGROUND

Where there is a lack of evidence, this must be shared with the donor so that consent is given freely and on the basis of the best information available. Rigorous assessment must be undertaken to determine the suitability to donate and to ensure that donor morbidity is kept to an absolute minimum. Consistent standards must be applied to donor assessment, which must remain robust, regardless of any imperative on the recipient side for the transplant to proceed. Transplant outcome should be optimised on the basis of what is best for the recipient, given that the patient is provided with realistic information to make a valid choice. With increasing expertise in the area, living donor kidney transplantation offers a real opportunity to extend the benefits of transplantation to patients who are traditionally considered to be 'high-risk' recipients, such as those with significant co-morbidity, the highly-sensitised, and older patients.

Living donor kidney transplantation has become well established in the majority of transplant centres across the UK. It demands the highest standards of clinical care and should be performed as part of a planned programme, with the full support of the clinical team and the infrastructure to underpin best practice. Potential donors and recipients should have access to local and international outcome data as an integral part of the decision-making process.

There are still challenges to be met. Achieving the national potential in living donor kidney transplantation, coherently and effectively requires further commitment and investment. The future legal framework will have some bearing on the direction of travel, especially in the context of unrelated donation, but it will primarily rest with individual centres to facilitate living kidney donation and to establish sustainable, clinically effective programmes. Added to this, with an increasingly informed public, patients will make choices about how and where they wish to be treated and we are obliged to consider how to realistically address this agenda.

1.2 PURPOSE OF THE GUIDELINES

This document provides updated and revised guidelines on all aspects of living donor kidney transplantation to assist health care professionals working in the field. It is in modular form to enable insertion of additional information, contemporary bibliography and modification of practice recommendations as appropriate and builds upon the original document published in 2000 in describing standards of clinical care and audit goals for practice in the UK. The document is designed to provide a comprehensive factual basis upon which robust local protocols may be drafted. Particular emphasis is given to donor evaluation and to ensuring that the donation proceeds under optimum circumstances. The statistical data and information provide the basis for achieving informed consent from both donor and recipient. As with the previous Guidelines, these are not intended to be didactic but define a contemporary framework for establishing best practice when used in conjunction with clinical experience and expertise.

1.3 REVISION AND PREPARATION OF THE GUIDELINES

The revised Guidelines were prepared by a multi-disciplinary working party of the BTS and RA and are based upon both the original document (2000) and a consensus view of the literature up to the date of publication (2005). They apply to kidney transplantation only. Sections have been added to give a broader perspective to some of the current challenges, societal responsibilities and contentious issues, for example, new surgical techniques; transplantation across HLA and ABO blood group barriers (6); the high risk recipient; the patient's view and donor re-imbursement. Where issues are still under consideration or discussion, for example, confirmation of the legislative framework and desensitisation protocols, modules will be amended or added as they become available and will be accessible via the BTS and RA websites.

Lisa Burnapp & Paul Lear, Editors

1.0 INTRODUCTION AND BACKGROUND

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2.0 LEGAL FRAMEWORK

Both the Human Tissue Act 1961 (HTA 1961) and The Human Organ Transplant Act 1989 (HOT Act)(1) and associated Regulations (1989 and 1998)(2-4) will be superseded by the Human Tissue Act 2004 (section 8), which received Royal Assent in November 2004, and will come into force in April 2006 (5,6). The Act is only applicable to England, Wales and N. Ireland. Separate legislation is being developed in Scotland.

2.1 THE HUMAN TISSUE ACT 2004

The Act outlines the legal framework governing the removal, retention and subsequent use of human tissue excluding gametes. Organ donation including living donation is included within this but is incorporated within the rules for tissue retention, including anatomical examination, post mortem and education.

The Act is drafted in wide terms, which are then qualified by excluding clauses and definitions. The Secretary of State is given broad powers to amend the Act through Orders and Regulations. The Act differs from preceding legislation including the Human Tissue Act 1961 (HTA 1961) and The Human Organ Transplant Act 1989 (HOT Act) in that the presumption is that the use of tissue is illegal unless:

1. Tissue is used for scheduled purposes
2. Appropriate consent is obtained.

Scheduled purposes defined in Part 1 of the Act include transplantation and organ donation.

2.2 THE HUMAN TISSUE AUTHORITY

The Human Tissue Authority will be the regulatory body that is established within the Act to regulate the use, storage and retention of tissue. The use of tissue for organ donation and transplantation will be incorporated within the remit of the Human Tissue Authority. The mechanisms by which the Human Tissue Authority will regulate organ donation and living donor transplantation are currently unclear.*

2.3 RESTRICITION ON TRANSPLANTS INVOLVING A LIVING DONOR

2.3.1 Prohibition of Commercial Dealings in Human Material

There are two separate areas of restriction, both creating criminal offences under Part 2 of the Act. Section 32, deals with organ trafficking and prohibits commercial dealings in human material for transplantation. Section 33 creates offences relating to the removal and transplantation of organs and other material from living donors except in specified circumstances, one of which may be where no reward has been given.

The following terms apply:

- “Transplantable material" is material of a description specified by regulations made by the Secretary of State.
- “Relevant material" is material, other than gametes, which consists of or includes human cells.
- "Advertisement" includes any form of advertising, whether to the public generally, to any section of the public or individually to selected persons, for reward.
- "Reward" means any description of financial or other material advantage.

2.3.2 Information about Transplant Operations

Section 34 of the Act states that the Secretary of State may make regulations requiring information regarding transplantation that have been, or are proposed to be, carried out to be made available to an appropriate designated authority.

* This Guidance will be updated once the requirements of the Human Tissue Act are clarified.

2.0 LEGAL FRAMEWORK

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3.0 ETHICS

The practice of living kidney donation has raised a wide range of ethical issues since its inception 50 years ago. With a major increase in the number of living donors there is a risk that these issues may be pushed aside and it is essential that all health professionals involved in living donor transplantation are fully aware of the general principles that underpin good ethical practice. A detailed description of the theoretical and philosophical background to the subject is beyond the scope of these guidelines but there have been several recent reviews (1-5). What follows is a summary, concentrating on the application in practice of the broader ethical concepts.

3.1 THE RECIPIENT PERSPECTIVE

The benefits of living donation to the recipient are detailed in the introduction and section 11 of these guidelines. They can be summarised as -

a) A better outcome than transplantation from deceased donors - regardless of the degree of genetic relationship or HLA mismatching between donor and recipient.

b) Avoidance of prolonged dialysis whilst waiting for a kidney from a deceased donor to become available - median waiting time for a deceased donor kidney in the UK currently ranges from 589 days for a blood group A patient to 1370 days for a blood group B patient (6). Time on dialysis is increasingly recognised as a risk factor for poorer outcomes after transplantation.

c) To facilitate the option of pre-emptive (pre-dialysis) transplantation.

d) The opportunity to minimise disruption to school, work and social life by having a planned procedure.

e) An increase in living donation increases the likelihood of transplantation for patients who remain on the list for a deceased donor transplant.

However, none of these benefits justify living donation unless the interests of the donor are given primacy.

3.2 THE DONOR PERSPECTIVE

Living donation involves a detailed process of investigation, major surgery, and a life thereafter with a single kidney. The published estimates of donor mortality are approximately 1:3000, the operation carries a risk of major morbidity of 1-2% and of minor morbidity of up to 20% (see section 6). Whilst laparoscopic surgery almost certainly reduces in-patient stay and post operative pain and allows the donor to resume normal physical activity (perhaps including return to work) more quickly than open nephrectomy, there is no data yet that suggest a lower mortality and limited data from randomised trials indicate that the incidence of complications is probably comparable between the two techniques.

It is therefore difficult on the surface to justify donor nephrectomy in the context of the well-known primary ethical priority to "do no harm". It is inevitable that removal of a kidney results in physical harm - to a lesser or greater extent - to the donor.

This dilemma is solved by involving another ethical principle, that of autonomy. This can loosely be interpreted as implying that the donor nephrectomy is morally acceptable when carried out with "informed consent, freely given" by the donor. This may be more difficult in practice than it sounds.

Whilst all living donor programmes would expect the donor to be given an appropriate, detailed description of the risks of donation, it is much less clear that all donors will listen. There is a well-described tendency for some people to decide at an early stage that they wish to donate and then to be impervious to or oblivious of any suggestion that they should make a more informed decision in the light of further counselling (7). The consent may be real but whether it is truly informed, may be questionable.

3.0 ETHICS

"Freely given" - who can truly know that, other than the donor himself? Whilst it may be possible to identify the donor who has clearly come under pressure or coercion, from either the recipient or from other family members, it seems almost inevitable that more subtle pressures exist in many situations that the donor does not reveal and that health care professionals do not detect. These may make it difficult or impossible for a potential donor not to proceed through the process.

It is important to recognise that there will be as many variations of "informed consent, freely given" as there are donor-recipient pairs, and in very many situations the motives and autonomy of the donor will be beyond question. Equally, because it may on occasions be more difficult to establish that consent is both informed and freely given, it is essential that this remains the standard to be applied to all potential living donors. It is for this reason that independence between the clinicians responsible for the donor and the recipient is recommended - allowing for, in effect, a donor advocate. A similar role may be played by a living donor co-ordinator, or more formally by an "independent third party" which may be embedded within the future regulations associated with the Human Tissue Act 2004 (see sections 2 and 4).

These principles have recently been re-stated in 'The Consensus Statement of the Amsterdam Forum on the Care of the Living Kidney Donor' (8) which sets out in a practical sense an appropriate expectation for an ethical approach to living donor transplantation.

Finally, it is important to recognise that the clinical team involved also has rights as well as responsibilities. If a fully informed donor wishes to proceed with a course of action that involves risks of mortality or morbidity more severe than the team find acceptable, they are under no obligation to proceed. Referral for a second opinion would be appropriate in such circumstances.

3.3 CONFIDENTIALITY

Maintaining confidentiality between donor and recipient and the respective clinical teams with responsibility for each is of primary importance, particularly because the uniqueness of the donor-recipient scenario creates a novel proximity between the two parties. Both donor and recipient have a right to a confidential relationship with their respective clinicians. It is important that the boundaries are made explicit from the outset and that there are realistic expectations on both sides about what information can be shared as a matter of course between all parties and what is confidential to each individual. It may be assumed that both parties have an equal right to information about one another but information should only be shared if express consent is given by either donor or recipient. It is advisable to have this discussion at an early stage and to ensure that the wishes of both donor and recipient are known to each other and to their respective clinical teams to avoid any possible misunderstanding.

The same principles should be applied to keeping and maintaining clinical records for recipients and donors. A separate clinical record should be maintained for each party. Some information will be shared on the basis that it is pertinent to both donor and recipient but this should be limited to that which is directly relevant to the management or performance of the transplant e.g. HLA mismatching/crossmatching results, CMV/EBV status (for post transplant prophylaxis or monitoring), ULTRA numbers, recipient diagnosis (for consideration of recurrent/ hereditary disease). It is accepted that essential information will be shared between clinical teams in the best interests of both parties when it has a direct bearing on the outcome of the transplant or donation (e.g. renal vasculature, renal function) and that access to such information via the transplant centre for the purposes of long-term follow-up should be made available.

3.0 ETHICS

There are no grounds for amalgamating complete recipient and donor records or for maintaining joint clinical documentation.

If a donor wishes to withdraw at anytime, the primary responsibility of the donor assessment team is to support him/her to do so; they should not feel under pressure to provide a 'medical reason' for withdrawal in order to offer the recipient a plausible explanation as to why the donor is 'unsuitable' (see section 4).

3.4 FUTURE PERSPECTIVES

It is expected that Codes of Practice, to be developed under the auspices of the Human Tissue Authority, will consider three forms of living donation not currently practiced in the UK (but increasingly being established elsewhere in the world).

3.4.1 Paired Donation

A donor-recipient pair (A) may be incompatible for blood group or histocompatability reasons. A second pair (B) may also be incompatible. However, donor A may be compatible with recipient B, and vice-versa. Whilst there may be practical and logistical issues complicating this procedure, such as the identification of suitable pairs and the desirability that the operations are performed simultaneously (to prevent one donor withdrawing consent after "his/her" recipient has received the transplant), there seem to be no fundamental ethical principles against such a procedure (9-10). Those units in Europe and the USA that have instituted programmes recently have only done so after extensive discussions and preparatory arrangements (11-13), and it seems likely that in the UK a national register of such potential pairs would be required, but a number of transplant units have already identified potential scenarios and it is to be hoped that authorisation will follow without undue delay.

3.4.2 Altruistic, Non-directed Donation

There are recent reports from the USA of kidney donation by altruistic living donors with no identified recipient - so called "good Samaritan" donation - the kidney being allocated through standard procedures to the most appropriate patient on the list waiting for a deceased donor transplant (14). Such donors have only been accepted after an intensive psychological/psychiatric screening process, and anonymity between donor and recipient has been essential. Whilst numbers to date remain small, the initial experience suggests that this can be an acceptable procedure and once again there seem to be no insuperable ethical barriers. Donor autonomy remains essential, and clearly the donor has none of the "indirect" benefits that occur following donation to a genetically or emotionally related recipient.

3.4.3 Incompatible Donor-Recipient Pairs

One group in the USA have started an alternative programme for incompatible donor-recipient pairs. The donor's kidney has been allocated to the most appropriate patient on the waiting list and in return the (incompatible) recipient has been given priority for the next available suitable deceased donor kidney. (11,12). This raises more difficult issues, as the donor could be described as receiving a benefit - not financial - in the priority given to the recipient, and furthermore the recipient is unlikely to receive a kidney that - physiologically - is as "good" as that from a living donor kidney.

If these strategies were to be adopted in the UK, they would be unlikely to yield more than a small number of donors per year.

3.5 THE YOUNG PERSON AS A LIVING DONOR

In England and Wales the legal position regarding consent by minors (under the age of 18 years) to medical treatment is determined in case law by '*Gillick*' (15). It could be argued that organ donation is not, *prima facie*, in the best interests of the minor as a potential donor, nor is it therapeutic treatment. However, if the young person is '*Gillick* competent' (understands fully what is proposed and is capable of making a choice in his/her best interests)

3.0 ETHICS

in principle, he/she may be able to consent to donation. Good practice demands that parental consent should always be obtained and, even if there is parental consent to donation, that an advanced ruling be sought from the High Court before proceeding under such circumstances, (16, 17). In Scotland, the Human Tissue (Scotland) Bill protects the position of children by providing that it should not be possible to remove an organ from a living child under the age of 16 for purposes of transplantation. To ensure consistency of approach across the UK, scrutiny of living donation is likely to be undertaken by the Human Tissue Authority established by the Human Tissue Act 2004.

The moral arguments for not subjecting young people, under the age of 18 years, to the rigours of living kidney donation are compelling and minors should rarely be considered as potential living donors unless sanctioned by the court. There are genuine concerns about autonomy and the validity of consent from minors in this situation. The British Medical Association considers that 'it is not appropriate for live, non-autonomous donors (minors) to donate non-regenerative tissue or organs'(18).

Summary point:
Individuals under the age of 18 years should rarely, if ever, be considered as potential living kidney donors unless sanctioned by the court.

3.6 THE BRITISH TRANSPLANTATION SOCIETY (BTS) ETHICS COMMITTEE

The BTS ethics committee is a subcommittee of the BTS Council. Healthcare professionals responsible for living donor kidney transplantation are encouraged to contact the Chairman of the BTS ethics subcommittee (via ethics@bts.org.uk) if they would like help or advice relating to the ethical aspects of a particular living donor recipient pair.

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4.0 INFORMING THE POTENTIAL DONOR

The General Medical Council (GMC) is explicit about the responsibility of registered doctors when seeking informed consent. Central to the validity of the process is the respect by the medical practitioner for the right of the individual to exercise autonomy and the provision of information in the form that allows them to make an informed decision.

4.1 INFORMED CONSENT FOR LIVING KIDNEY DONATION

The need for informed consent should be explained to the potential donor and he/she should be provided with information about living kidney donation in both verbal and written form. The mortality of living donor nephrectomy and the risk of short and long-term complications must be fully explained. The prospective donor should be given a realistic estimate of the likelihood of successful transplantation for the recipient. If there are factors that increase the risk of morbidity or mortality in the recipient these must be discussed openly with the donor, but only if the potential recipient has agreed to share this information. If the recipient is unwilling to share pertinent information, the donor cannot give valid consent.

Consent must be freely given and the consenting clinician must be satisfied that there is no defect in autonomy that could compromise the ability of the prospective donor to make a competent and cogent decision. The potential donor should be seen separately, in the absence of the prospective recipient and their family, and should be reassured that their views with respect to kidney donation, as well as their medical and social history will be treated in strict confidence (see section 3).

The option for the potential donor to withdraw with dignity at any stage in the preparation for donation, without having to provide an explanation for his/her action, must be made clear from the outset and he/she must be allowed adequate time to reflect on the decision to donate. A balanced view of the advantages and disadvantages of living donor transplantation must be provided. If after discussion, the donor decides not to proceed, the decision must be respected and should not be regarded as a failure but as a natural result of the informing process (1). If additional emotional support is required, this may be adequately addressed either within the transplant centre or in the primary care setting, without referral to a mental health professional. However, provision must be made to ensure access to specialist psychological/psychiatric services if referral is necessary (see section 4.4).

The prospective donor may be unable to donate for a medical reason or due to anatomical abnormality of the kidneys. Inability to donate may result in distress for both donor and recipient with resultant feelings of failure, anger at self and guilt that may lead to depression. Again, the need for emotional support must be anticipated and adequately provided for.

The decision to proceed with living kidney donation or not can be stressful for both donor and recipient and their respective family and friends. If several family members are contemplating donation, the decision making process as to whom should be considered as the preferred potential donor, may be complex. The healthcare team can assist by identifying and addressing the relevant issues at an early stage so that all parties can make a choice that is as fully informed as possible.

4.2 PATIENT ADVOCACY

In order to comply with current legislation, an independent third party is required to meet with both donor and recipient separately where an application to the Unrelated Live Transplant Regulatory Authority (ULTRA) is made (see sections 2 &3). This is separate from a formal psychological assessment but may, by coincidence, be performed by a mental health professional.

4.0 INFORMING THE POTENTIAL DONOR

As a matter of principle, the opportunity for the potential donor to meet separately with a third party who is independent of the transplant team such as a physician, family GP, psychiatrist/ psychologist or counsellor, is considered good practice but is not mandatory for scenarios that are not subject to the current legislation. However, the role of the independent assessor may be widened to include all living donor scenarios within the future regulations of the Human Tissue Act (see sections 2&3).

It is certainly essential that an informed health-care professional who is not directly involved with the care of the recipient acts as donor advocate in addressing any outstanding questions, anxieties or difficult issues and assists the donor in making a truly autonomous decision. It is important for the potential donor to understand that they are not the only source of a transplant. When a donor does not wish to donate, but is concerned that refusal may result in family conflict, the donor advocate should assist with discussions to limit damage to familial relationships (2). If at all possible, it is preferable to encourage open and honest discussion between donor and recipient from the outset. Pre-emptive discussion is helpful in ensuring that both parties are fully informed about how information will be handled by their respective healthcare teams and to minimise the risk of future conflict.

The recipient may be offered the option to meet separately with an independent and informed healthcare professional who can offer a different perspective from that of the nephrology and transplant teams. Such a meeting would provide an opportunity, free from pressure, to express thoughts regarding acceptance of the kidney. This is especially important in the case of young adults (3). It should not be assumed that all recipients wish to accept living donation and, provided that their decision is an informed choice, it should be respected. In such cases, they may need support and guidance to refuse the offer without causing the potential donor distress or relationship conflict.

4.3 INDEPENDENT INTERPRETERS

There is particular concern that donors who have a poor command of English and require an interpreting service in order to understand the questions and issues being put to them by clinicians may be open to coercion. Current legislation requires the use of an independent interpreter to protect the interests of the potential donor in this regard when making application to ULTRA. This is the best practice model for all cases where a translator is required. The translator should be unknown to both the donor and recipient and must be competent to discuss the implications and associated risks of donor nephrectomy and the post operative recovery process. They must be able to interpret accurately the breadth of discussion that may be required between the clinician and both parties. If these criteria are not met, the potential donor may be inadvertently misled or fail to comprehend fully what they are being asked to undertake.

Best Practice:
The donor must be offered the best possible environment for making a voluntary and informed choice about being a kidney donor. Independence between the clinical teams responsible for both recipient and donor is recommended to promote donor advocacy.

4.4 PSYCHOLOGICAL ISSUES

Psychological problems after donation are infrequent and most donors experience increased self-esteem, whilst donor and recipient relationships are enhanced. The majority of donors express no regrets after donation (4). However, early identification of pre-existing or potential psychological/ psychiatric issues that might arise for the prospective donor is essential to ensure that these are appropriately addressed.

Opportunity for the potential donor to raise psychological concerns and to discuss these

4.0 INFORMING THE POTENTIAL DONOR

in confidence with an appropriate member of the healthcare team should be offered as an integral part of the assessment process. Issues related to the decision making process and previous psychological problems should be explored, as should the donor's relationship with the recipient and within the context of the wider family. The purpose of such an assessment is to identify the level of support or intervention that may be required so that appropriate arrangements can be made, including referral to a mental health professional if necessary. A full psychological/psychiatric assessment should be sought if there is concern about the suitability of a donor on mental health grounds; for example, if there is evidence of previous or current mental illness, active substance abuse, dependence on prescribed medication, self-harming behaviour or significantly dysfunctional family relationships, particularly between recipient and donor. Such an assessment is valuable in establishing when it is unsuitable to proceed to donation on psychosocial grounds.*

Support will be provided by a variety of health-care professionals who have the necessary knowledge and skills to deal effectively with a range of psychological and social needs. Most transplant centres have designated personnel (usually, a transplant co-coordinator or nurse specialist) who play a key role in organising the assessment and surgery for donor and/or recipient. Such individuals generally become closely acquainted with the patients and their families and may be best placed to provide the necessary support, even in the context of adverse events prior to or following transplantation. Other centres have dedicated social workers, counsellors, psychologists and psychiatrists, or access to such colleagues, to whom patients can be referred for specialist intervention and additional support.

Not all donors and recipients will require referral to a mental health professional, but a clear, stratified framework for psychological care must be in place to ensure that needs are accurately identified and appropriately met and that there is access to a range of specialist services for patients who may need to be referred. The National Renal Workforce Planning Group recommends a 'tiered approach' to delivering support and psychological services (5).

Studies suggest that by merely presenting the option of living donation the potential donor is immediately placed under an unwarranted moral burden and, may feel in a 'no win situation' (6). If the potential donors say 'no', they may feel guilt, fear family conflict and regret the decision later, and if they say 'yes', they may cause conflict between the family of birth and the family of marriage and may regret the loss of an organ later. Whilst it may not be possible for the donor to avoid these pressures completely, a supportive environment, which encourages discussion can relieve the strain and facilitate decision-making.

Sibling decision-making has been reported as one of the most complex areas (5). Motivational factors such as altruism, manipulation of familial relationships, coercion and covert pressure are reported. Donor advocacy (see section 4.2) is essential to address these issues as robustly as possible.

The donor and recipient should be aware of psychological problems that have been reported after donation (7). These usually focus around the gift exchange elements of donation; recipients suffer psychological distress from feelings of indebtedness, which they can never repay, and donors exhibit proprietary interest in the health, work, and private life of the recipient that can cause damaged relationships.

**Based upon a protocol developed at the Royal Infirmary of Edinburgh: 'Triggers to Psychiatric Referral in Renal transplant Assessment'.*

4.0 INFORMING THE POTENTIAL DONOR

Such issues should be raised prior to surgery to pre-empt difficulties that might arise at a later date. In terms of psychological care, the impact of living donor transplantation for donor and recipient should be considered within the context of the wider family network to ensure effective support and intervention.

4.4.1 Death

The death of either donor or recipient following surgery is rare but has been reported. Studies show that there is a need for immediate bereavement support to help with resultant feelings of guilt, loss, anger and depression expressed by both the survivor and members of the family. Bereavement support in these cases should be provided by qualified, independent counsellors and should continue in the community for as long as required.

4.4.2 Transplant Failure

Early graft failure is again rare but will result in feelings of profound loss for many donors and recipients. Emotional support is essential at this time but studies show that with appropriate help the majority of donors and recipients recover from this disappointment without psychological morbidity (10). Support, up to and including referral to a mental health professional, if necessary, must be accessible to all patients and their families.

Best Practice:
Support for the prospective donor, recipient and family should be an integral part of the pre-donation/ transplantation process. Psychological needs should be identified at an early stage in the evaluation to ensure that appropriate support and/or intervention, up to and including referral to a mental health professional if necessary, can be initiated. Patients' needs vary and the provision of support and psychological services should be stratified accordingly. Access to specialist psychiatric/psychological services should be available for patients who need to be referred.

4.5 THE RESPONSIBILITY OF THE DONOR'S SURGEON

The surgeon performing living donor nephrectomy has a particular responsibility under his/her duty of care to ensure that the donor understands fully the potential risks and long-term effects of the operation. It is recommended that a combination of verbal and written information is given to potential donors and that the areas detailed in section 6 of this document are specifically addressed.

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5.0 PATIENT EXPECTATIONS: A PERSONAL PERSPECTIVE FROM A PREVIOUS DONOR*

Much of the information relevant to the recipient of a living donor kidney transplant will be provided as part of the assessment process for the transplant list. Further information, specific to a possible living donor transplant, would be provided by the clinician responsible for the care of the recipient and the broader healthcare team. However, it is essential that appropriate links are maintained between the staff responsible for the donor and the recipient, and that (within the limits of confidentiality) the recipient is fully informed of the progress of the donor work-up process. Separate arrangements would apply if "paired" living donation or "altruistic stranger" donation programmes are developed in the UK. The following comments refer primarily to the expectations of the living donor and should be read in conjunction with other relevant sections within this document.

5.1 INITIAL CONSIDERATIONS

5.1.1 Provision of Information and Planning

Once the possibility of living donation has been raised, there is a large amount of information for the prospective donor to consider. A number of strategies may ease this process, enabling the potential donor to understand the whole process at an early stage, identify any specific problems and place the process in an appropriate context with reference to work, family responsibilities and other issues.

a) The opportunity to talk to someone who has gone through the process of donation. 'One to one' discussions or meetings with previous donors, facilitated through the living donor co-ordinator is one of the most valuable ways to achieve this but patient group meetings or formal presentations to a number of potential donors may be preferred.

b) The availability of literature on the process of living donation, including the risks and benefits, with both national and local perspectives.

c) Provision of a flow-chart or algorithm that summarises the donor evaluation process up to and including the surgical procedure. This should reflect local practice and include detail about anticipated timeframes, numbers and duration of hospital visits and the potential impact on domestic or work arrangements for the donor and his/her family: in particular, any investigations that require an in-patient stay should be highlighted. Additional aspects to the process, (e.g. ULTRA or its successor) should be incorporated in the algorithm.

5.2 CLINICAL ASSESSMENT

The duration of the donor evaluation process should be appropriate for the particular donor and recipient pair, depending upon the complexity of the assessment and the optimum timing of the transplant, taking into account the needs/wishes of both parties. It is difficult to be prescriptive about timescales but, a straightforward evaluation for a donor living in the UK is unlikely to exceed 3 months and maybe performed more quickly if it can be arranged and the donor is willing.

5.2.1 Investigations

It is probably not necessary to provide detailed explanations of all donor investigations over and above the normal description and purpose of the tests, and their likely timescale.

5.2.2 Confidentiality

a) The donor assessment and investigation should be carried out through a confidential professional relationship with a clinician whose primary responsibility is for the care of the donor and who should not be the clinician who is responsible for the recipient and the transplant operation.

b) The option for the donor to withdraw from the process at any stage must be pre served. The reasons for such a decision should remain confidential between the potential donor and the clinician.

** written by a previous donor who offers a personal perspective on the expectations of the prospective living donor.*

5.0 PATIENT EXPECTATIONS: A PERSONAL PERSPECTIVE FROM A PREVIOUS DONOR*

c) The process should, as far as possible, be organised with the needs of the potential donor as a priority, particularly when the date for the operation is arranged.

5.3 IN-PATIENT CARE

5.3.1 Choice

Donor-recipient pairs are likely to vary in their wishes as to whether they are nursed in beds in close proximity to each other, or in different parts of the ward or hospital. Both options should be available. Again, different considerations would apply to "paired" or "altruistic stranger" donors.

5.3.2 Informing the Donor

Some donors are likely to find the ups and downs of the recipient's progress stressful. This is particularly so if further investigations - such as transplant biopsy - are required. Having due regard to patient confidentiality, and with the recipient's consent, clinicians should involve the donor in discussions concerning the recipient's progress as far as is practical and reasonable.

5.4 DISCHARGE ARRANGEMENTS

Arrangements for discharge from hospital should be co-ordinated by the donor and recipient clinical team(s). If the donor is to be discharged before the recipient, local "hostel-type" accommodation should be offered, to allow the donor to remain in close contact with the recipient with minimal travelling.

5.5 LONG-TERM CONSIDERATIONS

Following discharge from immediate surgical follow-up, all living donors should be reviewed clinically on an annual basis. This not only provides the necessary long-term data to inform future practice (see Section 9) but also provides reassurance to the donor that all is well.

5.6 SOCIO-ECONOMIC CONSIDERATIONS

It is important that the potential donor is given an early understanding of the possible financial and practical consequences of donation. This should include leave of absence from employment, possible loss of earnings, expenses incurred as part of the assessment process and the possibility of reimbursement of legitimate expenses. There may be anxieties about the validity of pre-existing life insurance polices during the immediate peri-operative period and the availability of new policies following donation. These issues should be relatively simple to resolve and it is recommended that they are addressed at an early stage in the process.

Paulette Cain, Previous Donor

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

6.1 INTRODUCTION

Living donor nephrectomy is a major surgical operation. This section covers the pre-operative care and preparation, the nephrectomy, and the early post-operative care of the donor. Responsibility for the donor lies ultimately with the surgeon performing the donor nephrectomy but optimal peri-operative care depends on an effective multidisciplinary approach that includes key contributions from nursing, anaesthetic, theatre, and ward nursing staff. The importance of effective communication between different team members cannot be over emphasised. Transplant units should have in place a written protocol detailing the peri-operative preparation and post-operative care of kidney donors. This should be reviewed annually and updated where necessary. The consent of the donor to undergo nephrectomy is made on the understanding that the operation will be performed by an experienced and competent surgeon and that all possible steps will be undertaken to reduce the incidence of peri-operative complications.

The risks associated with living kidney donation can be divided into the early risks associated with the donor operation (i.e. peri-operative mortality and morbidity) and the late or long-term risks of life with a single kidney. In the absence of national donor registries or large prospective studies with effective follow-up, the long-term risks of donor nephrectomy remain incompletely defined. There is, however, a wealth of retrospective evidence, which suggests that kidney donation is associated with a low level of medical risk in a healthy donor.

6.2 PERI-OPERATIVE MORTALITY

Estimates of living donor mortality are available from three large American surveys (covering nearly 10,000 operations) and numerous single centre reports (1-4). These studies are retrospective and the data may not be complete.

The reported death rates are variable but 1 in 3000 is accepted as an accurate assessment of peri-operative mortality. The most common causes of death being pulmonary embolus, hepatitis and cardiac events (myocardial infarction and arrhythmias) (2, 5, 6). It has been pointed out that these death rates are comparable with the risk in the USA of dying in a road traffic accident in one year (0.02%) (4). Prior to 1998, at least two peri-operative donor deaths were reported in the UK (7). One was due to myocardial infarction and one to pulmonary embolus. Since the inception of the UK Transplant Living Donor Registry in 2000, three deaths have been reported, from 3 to 18 months post nephrectomy, from a cohort of 958 donors (0.3%). Two were due to myocardial infarction/ischaemic heart disease (at 3 and 14 months) in donors who were 60 and 53 years of age respectively. A third death was due to cancer of the uterus (at 14 months) in a 67 year-old donor. No peri-operative deaths have been reported to the UK Living Donor Registry.

Summary point:
The peri-operative mortality rate for living donor nephrectomy is reported at 1 in 3000.

6.3 PERI-OPERATIVE MORBIDITY

The precise peri-operative morbidity of living donor nephrectomy is difficult to ascertain because some reports give overall complication rates whilst others present data relating to specific complications. Moreover, variations in the precise definition of specific complications may result in apparent differences in their incidence. This factor also affects the classification of complications into major and minor sub-groups. Notwithstanding these problems, the reported perioperative complication rates for living donor nephrectomy have been summarised for a large number of single centre studies (4). The mean overall complication rate was 32% and the major peri-operative complication rate was 4.4%.

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

The estimated 'major complication' rate in a survey by Bay and Hebert (3) was 1.8% whereas the American Society of Transplant Physicians (ASTP) survey (1) reported that 22 out of 9692 (0.23%) kidney donors experienced 'potentially life-threatening or permanently debilitating' complications. Kasiske et al (4) extracted data from a large number of published reports and calculated the reported rate (mean and SD) for specific complications.

In a review of 10828 living donor nephrectomies performed in the USA between 1/1/1999 and 1/7/2001 there was a 0.02% mortality with a further patient in a persistent vegetative state (8). The three donors concerned all underwent laparoscopic nephrectomy. Table 6.1. shows the incidence of complications for open nephrectomy and for laparoscopic hand-assisted and full laparoscopic nephrectomy. The previously described risk for open nephrectomy was 0.03%. This survey suggested that the mortality rate was unaffected by the introduction of laparoscopic nephrectomy. However, there was only a 73% response from centres surveyed and the authors suggest that the units with higher complication rates may have been less likely to respond. There does appear to be a higher frequency of bowel associated problems after laparoscopic nephrectomy although the numbers are small.

It is important to note that many of the studies quoted above were undertaken over a decade ago. In a single centre report of 871 kidney transplants performed between 1985 and 1995, two patients experienced a major complication (femoral nerve injury and a retained sponge requiring re-operation) (9). Sixty nine of the donors (8%) experienced a minor complication. The authors attributed the low complication rate in this large series to refinements in patient care and operative technique.

Donor nephrectomy is most commonly undertaken through a loin incision, although some surgeons prefer a trans-peritoneal approach. Irrespective of the type of incision, wound pain is a major source of anxiety for the donor (see section 6.8). The incidence of prolonged wound pain is difficult to determine but the figure of 3.2% reported by Cosimi (10) should be regarded as realistic. A small number of patients may require referral to a pain clinic.

Table 6.1 Complications following donor nephrectomy (8).

Complication	Open nephrectomy (5660) %	Laparoscopic hand assisted (2239) %	Full laparoscopic nephrectomy (2929) %
Re-operation	0.4	1.0	0.9
Complications not needing re-operation	0.3	1	0.8
Bleeding	0.15	0.18	0.45
Bowel obstruction	0.05	0.27	0.1
Bowel injury	-	0.1	0.14
Hernia	0.18	0.5	0.03
DVT/Pulmonary embolus	0.02	0.09	0.1
Pneumothorax	0.09	0.05	-
Prolonged ileus	-	0.05	0.06
Rhabdomyolysis	-	0.09	0.13

Readmission rate Open 0.6% Laparoscopic 1.6%

Summary point:
The major peri-operative complication rate for donor nephrectomy is approximately 2% and incidence of prolonged wound pain 3.2%

6.4 LONG TERM RISKS

6.4.1 Late Mortality

The evidence that provides a basis for counselling prospective living kidney donors about the long-term risk to health comes from two sources.

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

The first is the experience of children and young adults who have undergone unilateral nephrectomy: the children principally for tumour (11) and the young adults because of trauma in World War 2 (12). These data sets are of particular value because of the long duration of the follow-up. Follow-up of 111 children revealed no increase in the risk of hypertension or renal impairment up to 25 years after nephrectomy. A review of 62 ex-servicemen who underwent uninephrectomy at an average age of 25 years showed no increase in mortality rate after 45 years of follow up. Medical histories and blood pressure, as well as renal function, were assessed in 28 subjects. The prevalence of hypertension was not increased. Three individuals had renal impairment, but conditions other than uninephrectomy could have contributed. The authors concluded that uninephrectomy in young adults has few major adverse consequences over the subsequent 45 years. Both studies observed an increase in asymptomatic proteinuria.

The second and more pertinent source of data on the long-term effect of uninephrectomy comes from follow-up of living kidney donors. The worldwide experience documented in the medical literature is larger than that for uninephrectomy for pathological indications but, caution must be exercised when extrapolating from published series because adverse events may be under reported. The best quality information on late mortality following donor nephrectomy comes from Sweden (13).
A single unit in Stockholm performed 459 living donor nephrectomies over a 20-year period from 1964 onwards. All 430 donors still living in Sweden were traced and actual survival was compared to national mortality rates. The cause of death in the kidney donors was similar to that seen in the general population: most deaths were due to cardiovascular disease and cancer. Actuarial survival at 20 years was 85% compared to an expected survival rate of 66%.

This result suggests that in Stockholm the donor work up ensured that only healthy individuals proceeded to donation and encouraged the authors to select as a title for their publication 'Kidney donors live longer' (see section 7 for detail).

Summary point:
Donors who successfully complete the evaluation for living kidney donation have an above average life expectancy.

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6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

6.5 PRE-OPERATIVE CARE AND PREPARATION

6.5.1 General considerations

Living donation should be undertaken as a planned elective procedure. The prospective donor will commonly be admitted to hospital the day before surgery. It is important that they are admitted to and cared for within a ward that has nursing and medical staff experienced in the care of living kidney donors. Typically this will be the transplant unit or sometimes a general surgical or urology ward with the relevant expertise. Admission of the prospective donor and recipient to the transplant ward has the advantage that it allows them to visit each other more readily after the transplant operation.

Living donor transplantation from an adult donor into a child recipient demands special consideration (see section 14.0).

Children should undergo transplantation in a hospital with appropriate paediatric nephrological, anaesthetic and transplant surgical experience and facilities. It is desirable that the donor operation is undertaken in an adjacent hospital facility as this minimises disruption for the donor family and allows the donor and recipient to meet soon after surgery. However, the donor operation should be undertaken in an environment where appropriate expertise and facilities for adult surgery are available. If these are not available on the same site it may be necessary to transport the donor kidney between sites. In such cases the transit time should be minimised to prevent unnecessary ischaemic damage to the graft and theatre access carefully co-ordinated.

6.5.2 Risk and Prophylaxis of Venous Thromboembolism

Preoperative assessment of the risk of venous thromboembolism and use of appropriate prophylaxis is a crucial aspect of peri-operative care. In 1992 Najarian et al documented 17 donor deaths in the USA and Canada giving a mortality of 0.03% (1).

Seven of the deaths reported were attributed to pulmonary embolus (PE), giving a mortality of 0.01%. The surviving donors had a mean follow-up of 20 years. The use of thromboprophylaxis was probably limited. The risk factors for the development of venous thromboembolism are relatively well defined and those that are of most relevance to a healthy living donor are listed below (2, 3).

- Increasing age < 40 years annual risk 1:10000, 60-69 years annual risk 1:1000, (10 x baseline risk)
- Obesity (BM1 >30 = 3 x risk)
- Immobility (bed rest over 4 days)
- High dose oestrogens (50μg oestrogen or more per day)
- Previous deep-vein thrombosis (DVT) or pulmonary embolus (PE) (See below)
- Thrombophilia (wide variety with broad range of risk cited between 2 to 80 times that of background population)
- Varicose veins = 1.5 x risk
- Type of surgery and anaesthesia = 10 risk
- Non O blood groups = 2-4x risk

In the absence of specific thromboprophylaxis, hospitalised patients with a personal history of DVT or PE who undergo surgery are at 'high risk' of thromboembolism. The following data is taken from observational studies of such patients (3).

Asymptomatic DVT at screening	25%
Asymptomatic proximal DVT at screening	7%
Symptomatic DVT	6%
Symptomatic non-fatal PE	1-2%
Fatal PE	0.5%

There is a high risk (30% within 5 years) of developing further venous thrombo-embolism (VTE) after an idiopathic VTE. Potential donors who have a personal medical history of DVT/PE should not proceed to donation.

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

Potential donors with a family history (first or second degree relative) of VTE should be screened to exclude significant thrombophilias. In such cases, donation may not be precluded but advice from a haematologist should be sought.

Non-directed screening of all potential donors is not recommended as screening for thrombophilic defects in the general population, in the absence of a positive personal/family history, is unhelpful and potential donors may be excluded on spurious grounds (4).

Females on oestrogen treatment (contraceptive or hormone replacement therapy) should discontinue treatment at least one month before undergoing donor nephrectomy.

Early mobilisation should be encouraged after living donor nephrectomy. Patients undergoing major elective surgery are classified as 'medium risk' and published guidelines for the prophylaxis of venous thromboembolism in hospitalised patients recommend that such patients should, in addition to early mobilisation, be given specific prophylaxis (3). Effective prophylaxis in patients undergoing elective major general surgery can be achieved by subcutaneous low-dose standard heparin (5000 IU, 8-12 hourly) or subcutaneous low-molecular-weight heparins (LMWH) (given according to the manufacturer's guidelines). The latter have been shown to be slightly more effective in general surgery without increasing the risk of haemorrhage (5). Prophylaxis should continue for at least 5 days (the minimum duration in clinical trials) or until discharge from hospital if this is earlier.

Heparin induced thrombocytopenia (HIT) may occur in 3-4% of patients given prophylactic heparin and the platelet count should be checked every 2-3 days during prophylaxis. Heparin may also cause other allergic reactions and a rise in serum transaminase levels. Both Dextran 70 and aspirin are of limited efficacy in preventing DVT after general surgery (3) and are not recommended as alternatives to heparin prophylaxis in kidney donors.

Mechanical methods for prophylaxis include graduated elastic compression stockings (6) and intermittent pneumatic compression (IPC) devices. They are of proven efficacy in preventing DVT in moderate risk surgical patients but have not been shown in clinical trials to significantly reduce the risk of fatal pulmonary embolus. Above-knee stockings are preferred to below-knee for DVT prophylaxis (3). There are some historical reports of efficacy of elastic stockings in PE prophylaxis and evidence in patients undergoing cardiac surgery that a combination of IPC devices and unfractionated heparin reduce the risk of PE by 62% (from 4% to 1.5%) (3). Since mechanical methods may, without disadvantage, be combined with low dose or low molecular weight heparin prophylaxis, their use in all kidney donors is recommended.

If insertion of an epidural catheter is planned for post-operative pain control, a period of 4-6 hours should be allowed to elapse after giving unfractionated heparin (UFH) before inserting the catheter, or delay the first dose until after insertion/surgery, in order to reduce the risk of bleeding (3). Published guidance suggests that there is benefit in delaying the first dose of prophylactic low-molecular-weight-heparin until 6-8 hours post-operatively, with a minimum of 24 hours before the next dose is administered (3, 7). This provides effective prophylaxis without the risks of increased bleeding and has the added advantage of providing a 'heparin-free' environment for the insertion of the epidural catheter. The epidural catheter should be removed a minimum of 10-12 hours after the previous dose of heparin, with subsequent doses delayed until at least 2 hours after catheter removal. Greater vigilance must be exercised in administering anti-thromboprophylactic agents if trauma or bleeding occurred at the time of the catheter insertion.

6.5.3 Prophylactic Antibiotics

Living donor nephrectomy is a 'clean' surgical operation and the overall incidence of wound infection is usually less than 5%. The administration of prophylactic antibiotics would

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

not be considered necessary by many centres although they are used routinely or selectively by some centres to minimise would infection. The decision about whether to use prophylactic antibiotics should be taken locally and is likely to be influenced by local audit of the incidence of wound infection.

6.5.4 Marking the Side of Nephrectomy

Before the donor is transferred to the operating theatre, the skin should always be clearly marked by the donor surgeon (using an indelible pen) to identify which kidney is to be removed. This is necessary irrespective of the surgical technique to be used for undertaking nephrectomy.

6.5.5 Donor Blood Transfusion

Living donors may occasionally require blood transfusion during the peri-operative period and all donors should be 'group and saved' before proceeding to theatre, so that blood is readily available if required. They should be warned, as part of the consent procedure, that blood transfusion may be needed. If available, prospective donors may be offered the opportunity to have autologous blood transfusion.

6.6 DONOR NEPHRECTOMY

6.6.1 General Principles

The donor operation should be undertaken in the presence of a consultant surgeon (as principal operator or first assistant) and consultant anaesthetist. Dedicated daytime theatre lists should be available for the donor and recipient operation.

In the majority of UK centres the donor and recipient operations are undertaken synchronously in parallel operating theatres staffed by two full teams of theatre personnel. This arrangement is considered best practice. It minimises cold ischaemic time and ensures that the kidney is removed from the donor only after it has been confirmed that there are no unforeseen problems with the recipient that prevent implantation. Sequential donor and recipient operations are also acceptable and have been shown to give equivalent outcomes in several uncontrolled and one controlled series (8).

The results of imaging studies (hard copy or electronic copy of the images) used to define the renal vasculature should be available to visualise in the theatre by operating surgeons.

Living donor nephrectomy can be undertaken using one of several different surgical approaches, and these can be broadly divided into open nephrectomy and endoscopic (usually laparoscopic) nephrectomy. Irrespective of the surgical approach used, living donor nephrectomy is a challenging procedure and requires a high level of surgical expertise. When considering the choice of surgical technique for undertaking living donor nephrectomy it is important to consider the following :

- The risk of life threatening complications in the donor must be minimised.
- Donor morbidity must be minimised
- The integrity and function of the donated kidney must be preserved

6.6.2 Induction of Anaesthesia

After induction of anaesthesia, a urinary catheter should be inserted to allow accurate monitoring of urine output in theatre and over the first 24-48 hours after nephrectomy. Insertion of a CVP line and arterial line are not generally considered necessary, although some UK centres use them routinely for donor nephrectomy. After induction of anaesthesia the surgeon should oversee the positioning of the donor on the operating table, as correct positioning is critical for both open and laparoscopic nephrectomy.

6.6.3 Open Donor Nephrectomy

Traditionally, living donor nephrectomy is undertaken through a flank incision, using a retro-peritoneal approach. Rib resection is only undertaken to improve surgical access, when this is limited by donor body habitus. This technique has been shown over many years to

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

be safe and effective with a low peri-operative mortality rate, acceptable risk of peri-operative complications and excellent preservation of graft integrity and function.

However, the extensive loin incision may result in significant wound discomfort and a prolonged convalescence. Post-operative pain may be worse after rib resection (9). It is important to remember that for the donor, the prospect of wound pain is one of the most worrying aspects of the operation. Modern approaches to post-operative wound pain limit but do not completely prevent post-operative pain. A small number (up to 5%) of donors experience chronic wound pain which may necessitate referral to a pain clinic (10,11). Nerve damage may lead to muscle paralysis with bulging of the wound and this, or the appearance of the scar, may lead to a poor cosmetic result.

In a small number of centres, open donor nephrectomy is undertaken through a different approach from the standard loin incision. The anterior extra-peritoneal approach is preferred by some surgeons and is reported to provide good exposure of the kidney vasculature (12,13). Alternatively, living donor nephrectomy can be performed using a transperitoneal approach through a midline or transverse incision. Proponents of this approach maintain that it is associated with less wound pain than the loin approach, although it may expose the donor to the risk of intestinal obstruction as a result of peritoneal adhesions (14,15). A postal questionnaire of UK renal transplant surgeons in the year 2000 revealed that nearly all centres surveyed undertook open donor nephrectomy through a flank incision with or without rib resection (16). Only three of the 27 centres surveyed had used an anterior extra- or intra-peritoneal approach during the year of the survey.

The move towards minimal access surgery has led to the use in some centres of mini-incision living donor nephrectomy (17). The limited amount of published data suggests that mini-incision (7-10cm) may be a safe alternative to traditional open nephrectomy in selected donors, with better cosmetic appearance and a more rapid recovery than standard open nephrectomy. At present there is insufficient published data to assess this technique.

6.6.4 Laparoscopic Donor Nephrectomy

Since the initial report from John Hopkins Medical Centre in 1995 (31) laparoscopic donor nephrectomy (LDN) has been widely adopted as the standard surgical approach by many transplant units worldwide. LDN appears to be superior to the open approach with respect to post-operative pain, hospital stay and recovery time (19, 21, 25, 38). Laparoscopic and open donor nephrectomy have similar incidence of complications of around 1-2 % (28). There is a small risk of long-term bowel obstruction.

The overall costs of LDN are higher than for open nephrectomy because of longer operative time and costs of disposable laparoscopic equipment. Shorter hospital stay may to some extent compensate for the higher cost. Furthermore, early return to work should be considered in the economic equation.

Laparoscopic donor nephrectomy is a technically challenging procedure and should only be undertaken by surgeons experienced in advanced laparoscopic surgery and in open donor nephrectomy. On the evidence available it can be stated that both open and laparoscopic donor nephrectomy are safe and can be accomplished with minimal short- and long-term morbidities to the donor. The procedure of choice is the one that is well practised in each transplant centre. However, all prospective living donors should be at least informed of the potential techniques available to remove the kidney.

To date, there have been no randomised controlled trials to compare laparoscopic with open donor nephrectomy. With increasing popularity of LDN worldwide, the prospect of such a trial is diminishing. All published reports are prospective analysis of LDN compared with historical cohort of open nephrectomy.

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

6.6.5 Donor Complications

LDN is a transperitoneal procedure associated with increased risk unique to laparoscopic surgery. At induction of pneumoperitoneum, blood vessels and bowels are at risk of injury, while during surgery, injury to adjacent structures can occur. Post-operatively, patients are at risk of developing small bowel obstruction as a result of internal and port-site hernias. Reported operative complication rate ranges from 10% - 14% (21, 22, 24). The rate of conversion to open surgery ranges from 2% - 6% (21, 22, 24, 26, 36). The majority of cases were due to vascular injury and tended to improve with experience. The overall surgical complication rate of LDN is similar to that observed during open surgery (28).

6.6.6 Recipient Complications

Initial reports of LDN raised concerns regarding increased incidence of delayed graft function, (DGF), ureteric complications and vascular thrombosis. Incidence of DGF ranged from 0% to 6% of recipients (26, 29, 32). This has been attributed to decreased renal perfusion secondary to pneumoperitoneum and warm ischaemia time during removal of the kidney. Reduced renal perfusion can be minimised by optimal fluid load of the donor and the use of mannitol, frusemide and dobutamine. Warm ischaemia time (WIT) depends on experience and ranges from 2-10 minutes (22). WIT is shorter with hand assisted LDN (35, 38). Most comparative studies show that rate of DGF after LDN is not different from that observed after open nephrectomy and that WIT has no effect on the rate of serum creatinine decline in the donor or acute rejection rate (19, 25, 32, 33).

Ureteric complications reported after LDN include urine leak and ureteric necrosis and stenosis. This has been attributed to stripping of the periureteral vascular tissue and endobag injury. The former can be minimised by dissecting the ureter medial to the gonadal vein and the latter by careful insertion of the ureter into the endobag. The overall incidence of ureteric complications after LDN is approximately 3% and is similar to open donor nephrectomy (19, 29, 30, 33). Vascular thrombosis may be related to multiple arteries if dissection does not proceed to the aortic origin or if there is a short renal vein. The renal artery should be divided close to the aortic origin. Renal vein reconstruction using saphenous vein is rarely necessary. The gonadal vein should not be used for reconstruction, as it is friable. Mobilisation of the external iliac vein with ligation/division of the internal iliac vein may be needed occasionally in the recipient. The role of systemic heparinisation is not clear, full heparinisation, 3000-5000 units daily, or no anticoagulants have all been advocated without a sound evidence base.

6.6.7 Technique

The original transperitoneal technique is considered "pure laparoscopic", where the kidney is dissected and vessels divided laparoscopically, the kidney placed in a bag (endobag) and removed through a midline or Pfannenstiel incision. Recently, several modifications have been adopted and advocated by different centres. These include the retroperitoneal approach and the use of hand assistance (hand-assisted laparoscopic nephrectomy, (HA-LDN)).

HA-LDN appears to be a safe and effective variation of the standard LDN. It reduces some of the technical difficulties encountered in the pure laparoscopic approach, in particular dissection of the upper pole. HA-LDN may also reduce the learning curve and facilitate the wider application of LDN in the UK. The hand, in some cases, may limit the operative field and sleeve adjustment with each hand withdrawal can prolong the procedure.

The retroperitoneoscopic technique is preferred in some centres. It appears to be safe and efficient (9,18, 37). Hand assisted retroperitoneal nephrectomy has similar advantages to LDN in terms of minimal invasiveness and has the potential to be a shorter operative procedure.

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

6.6.8 Laparoscopic Right Donor Nephrectomy

Although laparoscopic donor nephrectomy was initially limited to the left kidney, the number of reported right donor nephrectomies has increased over the last few years (20, 27).

6.6.9 Vascular Assessment

Accurate arterial and venous anatomy is important to improve the safety of LDN and reduce vascular thrombosis. Left kidney with retro-aortic venous drainage should be avoided, as the renal vein is very friable. Commonly MRI or CT reconstructions are used. Spiral CT angiography is preferred because it provides superior imaging of the renal veins, particularly the left lumbar vein. (see section 7).

Best Practice:
LDN requires advanced laparoscopic skills and it should only be undertaken by surgeons who have a high level of competence in laparoscopic surgery and are fully familiar with the procedure. LDN has a steep learning curve and monitoring is obligatory.

The UK NHS National Institute of Clinical Excellence (NICE) issued its guidance on LDN in May 2004 (39). NICE concluded that current clinical evidence on the safety and efficacy of LDN appeared adequate to support its use in the NHS. The guidance stated that the transperitoneal approach is preferred because it allows more working space, makes it easier to remove the kidney and the incision is less painful. Bleeding, injury to adjacent structures and conversion to open nephrectomy were identified as the main safety concerns. In England, the Health Service Circular (HSC) states that any doctor considering the use in the NHS of a new interventional procedure which he/she has not used before, or only used outside the NHS, should seek the prior approval of their NHS Trust's Clinical Governance Committee.

UK centres proposing to introduce a LDN programme should ensure that arrangements for clinical audit of the procedure are in place and used to review the outcome of the procedure. An independent assessor from another centre is advisable if audit reveals cause for concern.

Patients offered LDN when it is being introduced for the first time should be made aware of the local experience as part of the consent process and this should be clearly recorded.

UK centres proposing to introduce a LDN programme should ensure that the entire team is adequately trained and should consider a mentoring programme with an UK unit in which the procedure has already been established.

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6.7 POST-OPERATIVE CARE

After nephrectomy, pulse, BP, pulse oximetry and urine output should be monitored regularly (hourly for the first 12 to 24 hours). Supplementary oxygen for 12 hours is routine. A major concern in the early post-operative period (up to 72 hours) is haemorrhage into the retroperitoneum after open nephrectomy and intraperitoneal haemorrhage after laparoscopic nephrectomy. The indications for surgical re-exploration because of suspected haemorrhage will depend on clinical findings. Following laparoscopic nephrectomy, the presence of marked peritonism after 24 hours, or prolonged ileus may indicate damage to intraperitoneal organs (particularly intestinal damage) and careful consideration should be given to early re-exploration.

6.8 PAIN MANAGEMENT POST NEPHRECTOMY

Optimum pain management for the donor is essential to encourage early rehabilitation and uneventful post-operative recovery.
This must be discussed with the donor during the assessment period to establish his/her expectations and understanding. Relevant information about the available options must be provided. The type of procedure, open or minimally invasive donor nephrectomy, may dictate analgesic requirements and hence the choice of pain relief that is used in the immediate post-operative period. Referral to the acute pain team, if there is one available, is helpful in optimising assessment and management of pain.

The alternatives include: (1)

1. Intravenous patient controlled analgesia (PCA) which is activated by the patient and enables opioid to be given via the intravenous route reliably and accurately in small bolus doses according to the needs of the patient.

2. Epidural analgesia, which is administered via an in-dwelling spinal catheter inserted into the epidural space immediately prior to induction of general anaesthesia, provides a maintenance dose of low dose anaesthetic and low dose opioid which is targeted at the site of the pain. Special arrangements must be made for training staff who are required to care for epidural infusions outside the critical care setting (see section 6.5.2 re thromboprophylaxis and epidural catheters).

Pain scores may be utilised to establish the severity of pain and to adjust dosing requirements.

PCA or epidural infusion should be administered peri-operatively so that pain is well-controlled when the donor regains consciousness post-anaesthesia. Anti-emetics may be required to control nausea and vomiting in the context of opioids.

Best Practice:
The donor should expect to be pain-free post nephrectomy. In order to promote optimum recovery, post-operative pain control must be planned with the donor during the pre-operative assessment period and the appropriate strategy adopted to ensure coherent pain management is achieved and tailored to the needs and preferences of the individual.

6.0 RISKS TO THE DONOR: PERI-OPERATIVE CARE OF THE DONOR AND THE DONOR OPERATION

The duration of PCA or epidural infusion will depend upon the individual but, in general, 24-48 hours should suffice, although this may be extended as required. Step-down analgesia should be administered in tandem with either of the above once oral fluids are tolerated so that intravenous/epidural requirements are reduced and can be discontinued without causing breakthrough pain. Step-down analgesia may include regular paracetemol combined with a non-steroidal anti-inflammatory drug (NSAID) such as ibuprofen or diclofenac if required. Codeine or tramadol provide an alternative to NSAIDs if preferred. The donor should be given an adequate supply of oral analgesia on discharge, according to need, and access to telephone advice as required. It is important to guard against constipation, which increases abdominal discomfort.

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7.0 - 7.7 DONOR EVALUATION

7.1 INTRODUCTION

The primary goal of the donor evaluation process is to ensure the suitability, safety and well being of the donor. This involves the identification of contraindications and unreasonable medical risks. In order to avoid important omissions, the evaluation of potential donors should be carried out according to an agreed, evidence-based protocol with which the donor assessment team is fully conversant. Investigations should be undertaken in a logical sequence so that the potential donor is protected from unnecessary procedures, such as invasive vascular imaging, until the appropriate time in the course of the assessment. There is good agreement regarding the routine screening tests that should be performed (1-4).

Throughout the evaluation, it is important to maintain good communication with the GP caring for the potential donor. This is more challenging if the donor is travelling from overseas and may not be possible in many cases. Where possible, the principle should be applied.

The stage during the donor evaluation at which to remove a recipient from the waiting list for a deceased donor kidney will vary according to individual circumstances and preference and should be decided after discussion with individual donor and recipient pairs. However, consideration must be given to the benefit afforded to the recipient from a living donor kidney in comparison with a deceased donor transplant, as well as to the optimal management of the transplant waiting list. Evaluation of potential living donors is a resource and labour intensive process. A large proportion of individuals who volunteer as donors will be found to be unsuitable for a variety of reasons including blood group incompatibility, a positive crossmatch test or the discovery of a medical contraindication during the evaluation process. Emphasis should be placed on the earliest possible triage of unsuitable donors to maximise benefit and to minimise risk for all parties concerned.

Strategies must be in place to offer appropriate follow-up for donors who are found to be unsuitable to donate.

7.2 ABO BLOOD GROUPING AND CROSSMATCH TESTING

ABO blood grouping allows the early identification of individuals who cannot donate because of ABO blood group incompatibility (5). It may be undertaken by the GP, or at a renal transplant assessment clinic. After blood group compatibility has been established, initial HLA typing +/- crossmatch testing should be performed in accordance with recommendations in section 8. Living donor transplantation across incompatible ABO blood groups can only be undertaken where there are specific protocols in place to support the management of the potential recipient (see section 12.1)

7.3 MEDICAL ASSESSMENT

It is important to manage the expectations of the donor from the outset and to emphasise the difference between a healthy individual and one who is suitable to donate. For example, a donor may be precluded from donation on the grounds of having a single kidney or multiple renal arteries, neither of which may be detrimental to his/her own health. The assessment may reveal previously undiagnosed disease and potential donors must also be warned of this possibility. The existence of a previously unrecognised condition may, for example, prejudice future attempts to obtain life insurance. However, there are some advantages to the potential donor if early detection of a health problem, which would otherwise have gone undiagnosed, can be treated.

A full medical history must be taken and the areas listed in Tables 7.3.1 should be specifically addressed.

7.0 - 7.7 DONOR EVALUATION

The history should also aim to identify any risks of latent or current infection in the donor that could be transmitted to the recipient by a kidney allograft (see Table 7.3.2 and section 7.19)

A rigorous clinical examination must be performed, taking particular account of the cardiovascular and respiratory systems and including the assessments listed in Table 7.3. 3.

A nephrologist should undertake the medical evaluation of the potential donor and, as previously noted, he/she should not have direct responsibility for assessing the medical suitability of the transplant recipient (6). It is accepted, however, that this is not always possible but it should be aspired to (see sections 3 and 4). Table 7.3.4 details the routine screening investigations that should be performed on the potential donor. If the donor gives a history of significant medical problems that are not directly related to the nephrological evaluation, then a specialist opinion must be sought.

Table 7.3.1

Points of particular importance when obtaining the medical history of a potential kidney donor

Haematuria/oedema/urinary tract infection
Nephrolithiasis
Ischaemic heart disease
Cardiovascular risk factors
Hypertension
Diabetes mellitus, including family history
Previous jaundice
Thromboembolic disease
Previous malignancy
Chronic infections such as tuberculosis
Systemic disease which may involve the kidney
Family history of a renal condition that may affect the donor
Smoking
Problems with alcohol or drug dependence
Psychiatric history
Obstetric history
Residence abroad
Previous medical assessments for life insurance

Table 7.3.2

History with respect to transmissible infections

Previous illnesses:
Jaundice
Tuberculosis and atypical mycobacterium
Malaria
Family history of mycobacterium tuberculosis
Family history of Creutzfeldt-Jakob disease (CJD), previous treatment with natural growth hormone, or undiagnosed degenerative neurological disorders
Specific geographical risk factors: e.g.
- Fungi and parasites
- Tuberculosis
- Hepatitis
- Kaposi's sarcoma
- Malaria
- Worms

7.0 - 7.7 DONOR EVALUATION

High risk of Hepatitis B & C, HIV, HTLV1 and HTLV2 infection
Drug addiction
Sexual partners of drug addicts
Female sexual partners of men who have had sexual relations with another man
Sexual partners of an HIV positive individual
Those who have paid for or been paid for sex within the last 2 years
Sexual partners of an indigenous African within the last 2 years
Homosexuals
Haemophiliacs and their sexual partners

Table 7.3.3
Points of particular importance when undertaking clinical examination of potential kidney donors
Body mass index
Blood pressure measurement
Examination of the cardiovascular and respiratory system
Examination for abdominal masses or hernia
Examination for lymphadenopathy
Evidence of self-examination of the breasts
Evidence of self-examination of the testes

Table 7.3.4
Routine screening investigations for the potential donor
Urinalysis
Dipstick for protein, blood and glucose
Microscopy, culture and sensitivity
Measurement of protein excretion rate

Blood tests
Haemoglobin and blood count
Coagulation screen (PT and APTT)
G6PD deficiency (where indicated)
Sickle cell trait (where indicated)
Haemoglobinopathy (where indicated)
Thrombophilia screen (where indicated, see section 6.5.2)

Creatinine, urea and electrolytes
Liver function tests
Bone profile (calcium, phosphate, albumin and alkaline phosphatase)
Fasting plasma glucose
Glucose tolerance test (if fasting plasma glucose 6-7 mmol/l)
Fasting lipid screen (if indicated)
Urate
Thyroid function tests (if strong family history)
Pregnancy test (if indicated)
Men >60yrs Prostate Specific Antigen (PSA)

7.0 - 7.7 DONOR EVALUATION

Virology and infection screen (See section 7.19 for detail)
Hepatitis B and C
HIV
HTLV (if appropriate)
Cytomegalovirus
Toxoplasma
Epstein-Barr virus
Syphilis
HHV8 (where indicated)
Malaria (where indicated)
Trypanozoma cruzi (where indicated)
Schistosomiasis (where indicated)
Strongyloides stercoralis (where indicated)

Cardiorespiratory system
Chest X-ray
ECG
Cardiovascular stress test (as routine or where indicated)
ECHO (where indicated)

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7.4 ASSESSMENT OF RENAL ANATOMY

The renal anatomy must be assessed to confirm the presence of two kidneys of normal size and to identify abnormalities such as a duplex collecting system, hydronephrosis, pelvi-ureteric junction obstruction and calcification in the urinary tract.

Abdominal ultrasound has the advantage of avoiding exposure to radiation but some clinicians prefer an intravenous urogram (IVU) as this may allow more accurate delineation of the pelvicalyceal and ureteric anatomy and also provides limited information about excretory function. Anomalies of the renal collecting system occur in less than 1% of individuals and an IVU may be unnecessary if spiral CT angiography or an angiogram with late films is employed (1,2). The presence of a duplex collecting system is not a contraindication to donation and if double ureters are present in one kidney, the contralateral kidney may be the most suitable choice for transplantation.

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7.0 - 7.7 DONOR EVALUATION

7.5 ASSESSMENT OF RENAL FUNCTION

For a potential kidney donor, a major area of concern is whether donation will cause impaired kidney function. Accurate measurement of renal function in a prospective donor is, therefore, important primarily for ensuring adequate residual kidney function in the donor but also to secure sufficient graft function in the recipient following transplantation. However, this is one of the most challenging areas of donor assessment. There are various pieces of evidence available to inform this process but none are absolute, nor have they been tested in a randomised trial.

Data from cross-sectional studies show that there is a wide range of 'normal' renal function and beyond 40 years of age this declines in a predictable manner. When evaluated according to the British Nuclear Medicine Society Guidelines (1) the mean GFR in young adults of both sexes is 103ml/min/1.73 m^2 with a decline of 0.9 ml/min/1.73m^2 per year after the age of 40 (2).

The data that is available from living donors suggests two things. The first is that across a broad age range (19-61 years), the remnant kidney increases its activity to provide a GFR of approximately 75% of the combined value that both kidneys had before donation (3). Secondly, the rate of decline in kidney function after donation is neither more or less marked than that seen in individuals with two kidneys (4). Special consideration may be needed when assessing kidney function in older donors as the degree of recovery of post-nephrectomy GFR may be less than that for younger people but there is not a significant body of evidence available for patients over the age of 60.

The aim of any guideline for donor GFR must be based upon the premise that an individual in his/her lifetime will not develop clinically significant renal impairment as a result of unilateral nephrectomy. On this basis, the potential kidney donor must have sufficient kidney function prior to donation to have an effective GFR at the age of 80 years, independent of the age at which he/she donated. Table 7.5.2 gives the values for GFR and age that will leave a GFR of 37.5 ml/min/1.73m^2 at the age of 80, given the reduction in GFR due to donation and the annual decline, as above. This threshold is shown plotted as the red line in Figure 7.5.1. This correlates closely with previous guidance based on smaller studies, which has supported practice to date (5).

The most accurate assessment of glomerular filtration rate (GFR) is achieved using radioisotopes such as ^{51}Cr-EDTA and this is recommended in all potential donors. Alternative methods based upon serum creatinine concentration are not sufficiently accurate in this context and measured creatinine clearance, using timed urine collections, is susceptible to considerable inaccuracy.

The divided renal function can be measured by combining a ^{51}Cr-EDTA GFR measurement with a ^{99m}Tc-DMSA scan of the kidneys (6). This information is advisable before nephrectomy if there is considerable disparity in the size of the kidneys or anatomical abnormality is noted but is otherwise not indicated. When renal function is normal but there is a significant difference in function between the two kidneys, the kidney with lower function should be used for transplantation.

7.0 - 7.7 DONOR EVALUATION

Figure 7.5.1

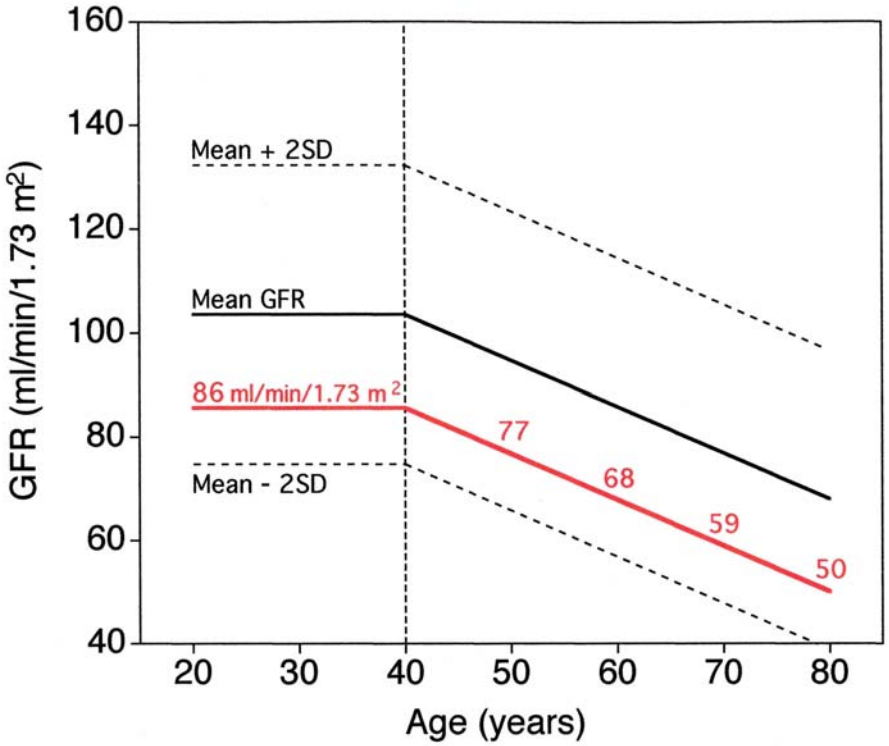

Figure 7.5.1: Diagram showing the variation with age of mean GFR (solid black line). The outer dashed lines show the ± 2 population standard deviation limits. GFR is constant up to the age of 40 years and then declines at the rate of 9ml/min/1.73 m² per decade.
The reference plot is based on an analysis of data for 428 live renal transplant donors [2] who had ^{51}Cr-ETDA GFR measurements performed according to the method described in the British Nuclear Medicine Society GFR guidelines [2]. The red line shows the safety limit of 86ml/min/1.73 m² for young adults declining to 50ml/min/1.73 m² at age 80. For transplant donors with pre-operative GFR values above the red line the GFR of the remaining kidney will still be greater than 37.5ml/min/1.73 m² at age 80.

Table 7.5.2 Acceptable GFR by Donor Age Prior to Donation

Donor Age (years)	Acceptable corrected GFR prior to donation (ml/min/1.73m²)
Up to 40	86
50	77
60	68
70	59
80	50

Best Practice:
GFR should be measured using an is topic marker: A prospective donor should not be considered for donation if the corrected GFR is predicted to fall below an effective measurement within the lifetime of the donor. A predicted GFR of 37.5 ml/min/1.73m² at the age of 80 is recommended as a minimum standard. There is a lack of evidence available for this for donors over 60 years of age.

7.0 - 7.7 DONOR EVALUATION

7.5.1 Renal Function Post Nephrectomy

Isolated cases of end stage renal failure in kidney donors have been reported despite satisfactory evaluation of renal function prior to donation (7-11). A survey of North American units carried out by the ASTP revealed 15 donors with renal impairment, of whom 11 were on dialysis (12). None of them had evidence of renal disease before kidney donation. Most developed *de novo* renal disease and the reported frequency of end stage renal failure in the donor population overall is less than that seen in the general population.
Fehrman-Ekholm found in the 402 donors assessed that there was a decrement in renal function compared to age and sex matched members of the population but this did not relate to the duration after nephrectomy, indicating no accelerated loss of kidney function (4). Goldfarb et al demonstrated that in 70 patients with a mean follow-up of 25 years that the average creatinine clearance was 72% of that prior to nephrectomy (6).

Summary Point:
A living kidney donor with normal renal function prior to donation is at no greater risk than an individual in the general population of developing end stage renal disease post unilateral nephrectomy.

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7.6 DEFINITION OF RENAL VASCULAR ANATOMY/ANGIOGRAPHY

The anatomy of the renal vasculature should be defined by an appropriate imaging technique. Approximately 25% of potential donors will have multiple arteries to one kidney and around 7% will have multiple vessels to both kidneys (1). A donor kidney with a single renal artery should, whenever possible, be chosen for transplantation. If both kidneys have single vessels, the left kidney is usually selected for donation because the longer renal vein facilitates implantation.

When the recipient is an infant or small child, some surgeons prefer to use the right kidney to facilitate intra-abdominal implantation. Multiple renal arteries are associated with an increased incidence of acute tubular necrosis (ATN) and urinary fistula (2,3) but do not adversely influence recipient or graft survival (4).

7.0 - 7.7 DONOR EVALUATION

It may be acceptable to use a kidney with multiple renal arteries for transplantation, provided that the surgeon responsible has the necessary experience in reconstructing the vasculature of the graft. It is helpful to identify early arterial bifurcation and short renal arteries, which can make donor nephrectomy more difficult. At least 14mm of main stem renal artery is needed to provide a single vessel for anastomosis and safe haemostatic ligation/ clipping in the donor. Renal arterial aneurysmal or occlusive disease and unsuspected parenchyma abnormalities may also be revealed. Another important goal of the vascular assessment is to ensure that the donor's remaining kidney is anatomically normal.

Renal angiography is the traditional method used to assess the renal vasculature. The current standard technique is transfemoral intra-arterial digital subtraction angiography (IA DSA), with or without selective vessel catheterization (5). The complication rate of arteriography has fallen in recent years because of the use of smaller catheters and reduced contrast volumes. The major complication rates (including thrombosis, peripheral embolism, false aneurysm and aortic and renal arterial damage) should be below 0.5% and even down to a level of 1 in 1000 procedures in the best hands (6). The reported rate for minor complications is 1-5% and the most common problems are haematoma and prolonged bleeding from the puncture site. Other disadvantages of conventional angiography are the exposure to radiation, which will be greater with selective vessel catheterisation, and the use of potentially toxic contrast medium.

Spiral computed tomographic angiography (spiral CTA) and gadolinium-enhanced magnetic resonance angiography (MRA) are newer techniques for vascular imaging which can be used as alternatives to conventional angiography for the pre-operative evaluation of donor vascular anatomy. They are less expensive and can be performed more quickly than conventional angiography.

CT angiography techniques have improved with the advent of multi-slice CT and are now widely available. The advantages of this procedure are that it is non-invasive, it has accuracy of approximately 96 to 98% compared with operative findings (7,8) and scans can be performed in a single breath-hold. CT can also detect other renal and vascular abnormalities, which may be relevant in the context of kidney donation. In the case of spiral CT angiography the pelvicalyceal system and ureteric anatomy is also imaged thereby avoiding the requirement for an IVU. It may also be used to measure GFR with the same accuracy as isotope GFR at the same session as vascular imaging (9). Exposure to radiation and use of IV contrast medium are relative disadvantages of this technique. Spiral CTA can be used to create a three-dimensional reconstruction of the renal anatomy which makes it the preferred choice for surgeons performing laparoscopic donor nephrectomy. In this situation the pre-operative identification of posterior lumbar tributaries of the renal vein is very helpful.

Gadolinium enhanced 3D MR angiography as an alternative technique has the advantage of avoiding ionizing radiation and uses a smaller dose of contrast. Not all patients are suitable for MR imaging however and there is evidence that small accessory vessels may not be detected as accurately as in CT or conventional angiography (10).

Summary Point:
Although conventional intra arterial DSA is the gold standard in terms of accuracy, the choice of imaging will depend upon local expertise and imaging modality available. Multi-sliced CT angiography is the preferred imaging technique for minimally invasive donor nephrectomy procedures because of the superior resolution of the renal vasculature.

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7.0 - 7.7 DONOR EVALUATION

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7.6.1 Reno-vascular Disease

Reno-vascular disease due to fibro-muscular dysplasia (FMD) is more prevalent in the general population than the majority of clinicians recognise. In normotensive individuals screened as potential transplant donors it probably represents 5% of the population (1, 2). For a living donor programme this is an issue that needs to be addressed. The literature is controversial as to what outcome a normotensive individual with FMD might expect (2). It is also unclear what the consequences maybe for the future if the disease is unilateral. Transplantation of a kidney with FMD is disadvantageous to the recipient, reported as a result of an inadvertent transplantation of a deceased donor kidney with FMD (3). Angioplasty or bench surgery to the FMD kidney prior to transplantation is a reasonable course. Provided that the donor and recipient are informed of the lack of knowledge in this area, it is reasonable to use a kidney with FMD for living donor transplantation (4).

Best Practice:
Atherosclerotic reno-vascular disease is a contra-indication to living donor kidney transplantation. FMD in the donor need not preclude donation but both donor and recipient must be made aware that there is little outcome data available.

Atherosclerotic reno-vascular disease is almost invariably associated with severe vascular disease and a higher mortality than for individuals without atherosclerotic reno-vascular disease (5). The risk to the donor is significant and these kidneys should not be used for transplantation.

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7.0 - 7.7 DONOR EVALUATION

7.7 DONOR EVALUATION: SUMMARY

- ***The suitability of the potential recipient for transplantation should be established prior to the evaluation of a prospective donor.***
- ***Donor assessment should be planned to reflect the wishes of the donor as far as possible and to minimise inconvenience to him/her. Flexibility in terms of timescales, planning consultations, attending for investigations and date of surgery is helpful.***
- ***The assessment process should be achieved in a focused, coherent fashion. Good communication between all parties is important and may be achieved most effectively by a designated co-ordinator. The results of investigations should be relayed accurately, appropriately and efficiently to the potential donor. Emphasis should be placed on identifying unsuitable donors at the earliest possible stage of assessment. There are challenges to be met when dealing with donors from over seas and with families for whom English is not their first language. Appropriate provision should be made to maximise communication under these circumstances.***
- ***A policy should be established for managing prospective donors who are found to be unsuitable and provision should be made for appropriate follow-up and support.***
- ***The organisational details for evaluating a prospective donor will vary between centres, reflecting available resources and personnel. Evaluation should be undertaken according to an agreed protocol and emphasis should be placed upon the appropriateness and progression of assessment rather than the specific manner in which it is conducted.***

7.0 - 7.7 DONOR EVALUATION

Table 7.7.1 shows a suggested model for donor evaluation.

Table 7.7. 1: Donor Evaluation: Summary and Organisational Chart

Early education & discussion with all potential transplant recipients +/- potential donors about optimal options for transplantation.

RATIONALE: **To promote planned, pre-emptive LD transplantation as the treatment of choice for suitable transplant recipients.**

↓

Establish recipient fit for transplantation & initiate appropriate pre-transplant assessment as per local protocol

RATIONALE: **To optimise management of recipient & donor(s) expectations. To avoid unnecessary investigative assessment/inconvenience for the prospective donor if transplantation cannot proceed.**

↓

Potential donor(s) identified.
ABO compatibility +/- HLA sensitisation confirmed. Primary contra-indications identified from donor(s) previous medical history. Confirm legal requirements can be met.

RATIONALE: **To initiate early triage of unsuitable donors.**

↓

LD Co-ordinator facilitates initial discussion with potential donor(s), +/- recipient & other family members as appropriate. If more than one potential donor, the most appropriate should be identified, taking into account possible social, psychological and medical risk factors.

RATIONALE: **To minimise evaluation of multiple donors & maximise best use of local resources.**

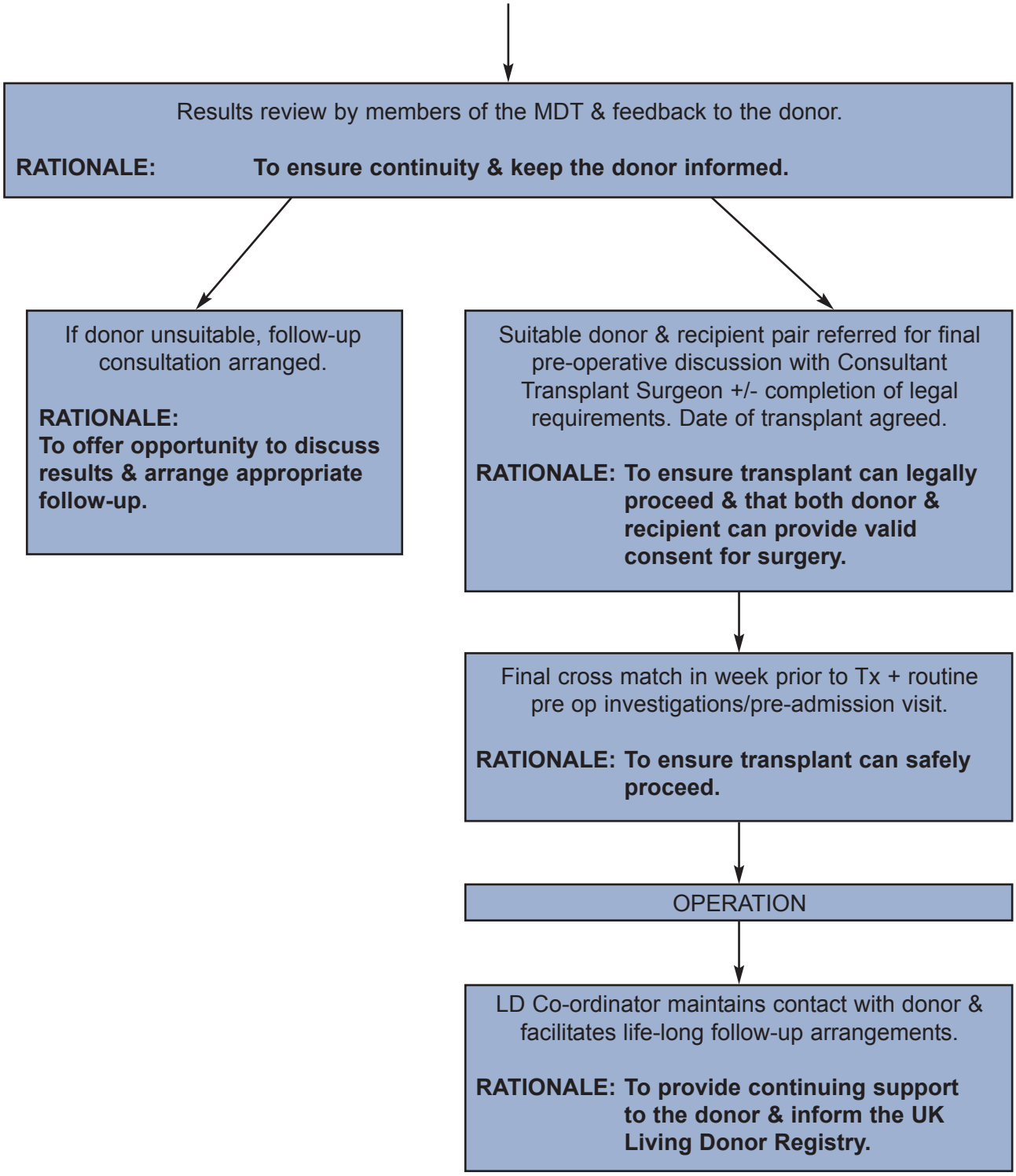
↓

Donor evaluation is planned in conjunction with the prospective donor, in a timely & appropriate manner, to an agreed protocol & in accordance with the availability of local resources. Emphasis should be placed upon a coherent, consultant led service with a logical progression of assessment using 'gold standard' investigative procedures, multi-disciplinary input & excellent communication between all parties.
A designated LD Co-ordinator is considered optimal.

RATIONALE: **To provide a clinically effective service based upon the best evidence available & national best practice guidelines.**

7.0 - 7.7 DONOR EVALUATION

Table 7.7.1: Donor Evaluation: Summary and Organisational Chart (Continued)



7.8 DONOR EVALUATION: DONOR AGE

The young and the old each raise different issues with respect to consideration as potential living kidney donors (1). The constraints on the use of minors and young people as living donors are addressed in Section 3. For older donors (> 60 years) a number of issues need to be considered. First, increasing age may be associated with more co-morbidity such as hypertension and diabetes, which might preclude donation (2). When considering older donors the medical evaluation, especially that of the cardiovascular system, needs to be particularly rigorous. Many centres consider stress cardiac testing to be mandatory when evaluating older potential donors. In addition post-operative complications after nephrectomy may be increased. Johnson et al reported no increase in the incidence of post-operative complications when older donors were used (3). Fauchald, on the other hand, reported a higher incidence of post-operative complications (cardiac complications and pneumonia) in donors over the age of 60 years (4).

A further concern regarding the older donor is the suggestion that kidneys obtained from older living donors have a worse outcome after transplantation (4) Renal function declines progressively with age and kidneys from older living donors have reduced function (5). However, the majority of studies suggest that both short-term and medium-term (5 years) graft survival rates are similar for kidneys from older (over 55 years) and younger donors (6-8). Data from the UNOS database has revealed that kidneys from donors over 60 years of age accounted for only 3% of first living donor transplants and their 84% 5-year graft survival rate was comparable with that of younger donor kidneys (9). Similarly in a recent study, 5 year graft survival after living donor transplantation was 76% for kidneys from older (over 60 years) donors (n=241) and 79% for kidneys from younger (aged less than 60 years) donors (n=518). However, serum creatinine levels remained significantly lower in the recipients of kidneys from younger donors and beyond 5 years their graft survival was significantly better (7). Another recent study found that, in the absence of acute rejection, kidneys from older living donors fared as well as those from younger donors (10). Overall, if the renal function of the donor is normal, after correction for age and gender, available evidence suggests that older donors should not be discounted on the basis of age alone. Older donors are more likely to be excluded from donating on the basis of problems discovered during the medical evaluation. However, each case should be considered on individual merit and if the older donor is judged fit after rigorous medical evaluation, there is no evidence for excluding donation on the basis of chronological age alone (3, 11, 12).

Best Practice:
Age alone is not an absolute contraindication to donation but the medical assessment of older donors (>60 years) must be particularly rigorous to ensure that they are suitable. Both donor and recipient should be made aware that the older donor may be at greater risk of peri-operative complications and that the function and possibly the long-term survival of the graft may be compromised.

7.8 DONOR EVALUATION: DONOR AGE

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7.9 DONOR EVALUATION: DONOR OBESITY

A body mass index (BMI) of more than 35 kg/m^2 should be regarded as an absolute contra-indication to kidney donation and a BMI of more than 30 kg/m^2 is a relative contra-indication. This seems to be a prudent approach based upon available evidence. The prevalence of adult obesity defined as a body mass index of greater than 30 kg/m^2 in England has increased markedly in recent years: 16% of men and 17% of women are classified as obese (1). Obesity is generally considered to be at least a relative contra-indication to living kidney donation. It is an independent risk factor for cardiovascular and respiratory disease as well as diabetes and the development of proteinuria (2-4). Praga et al found that 92% of patients with a BMI of greater than 30 at the time of nephrectomy developed proteinuria or renal insufficiency (5). At 10 years post nephrectomy 60% of individuals had proteinuria and 30% renal insufficiency as defined by a serum creatinine of 124 mcmol/l and a clearance of less than 70 mls per minute per 1.73 m^2. Obese patients are at increased risk from peri-operative complications during and after major surgery, particularly pulmonary embolism, respiratory complications and wound infection (6, 7). In addition to the short term risks, obesity will, in the long term, compound the risk of hypertension (see section 7.10) and diabetes (see section 7.11).

A recent single centre study compared the outcome of 107 obese living donors (BMI > 27 kg/m^2) with 116 non obese donors (BMI < 27 kg/m^2) (7). The overall peri-operative complication rate was significantly higher in the obese donors (17% versus 3%). The majority of complications were wound related. By contrast another recent single centre report of 871 donor nephrectomies, a BMI of > 30 kg/M^2 was not a significant independent risk factor for peri-operative complications (6).

More recently obesity has been recognised as a risk factor for the development of progressive renal injury (8,9). The prevalence of obesity related renal disease, which may lead to ESRD has increased by ten fold over the last 15 years although the absolute incidence remains low (10). The impact of nephrectomy in obese individuals has been studied in a retrospective analysis of 73 patients who underwent nephrectomy (5).

Of these 73 patients, 20 patients developed proteinuria (3g/day) approximately 10 years following nephrectomy and 13 of these developed renal insufficiency. Retrospective comparison of patients prior to uninephrectomy was made between the 20 patients who developed proteinuria versus the 53 patients who did not develop proteinuria. It was also noted that 92% of patients with BMI greater than 30 kg/m^2 developed proteinuria. These findings suggest, but do not prove, that nephrectomy in patients with obesity leads to the development of proteinuria.

Best Practice:
Obese patients with a body mass index greater than 30 kg/m^2 should undergo careful pre-operative evaluation to exclude cardiovascular, respiratory and renal disease. They should be counselled regarding the increased peri-operative risk and potential long-term risk of renal disease and advised to lose weight prior to donation and encouraged to achieve their ideal weight following donation.

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7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR

7.10.1 Definition of Hypertension in a Potential Kidney Donor

Hypertension is one of the most common reasons for declaring a potential kidney donor medically unsuitable (1). In this section, the definition of hypertension is considered in the context of kidney donation, together with the effect of donation upon blood pressure in the treated hypertensive patient.

There is a continuous relationship between blood pressure level and cardiovascular risk and in normal clinical practice clinicians are interested in a definition of hypertension such that any morbidity associated with anti-hypertensive treatment is outweighed by the benefit in terms of reduced cardiovascular risk.

Recently updated guidelines from the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (2), British Hypertension Society (3) and European Society of Hypertension guidelines (4) arbitrarily define adults with blood pressure of 140/90 mmHg as hypertensive in the absence of other cardiovascular risk factors or evidence of target organ damage. However, it is important to note that the need for anti-hypertensive treatment must be considered in terms of the perceived total risk of cardiovascular disease (2,3,4).

The morbidity from cardiovascular disease increases with blood pressure values that are still within the "normal range". The 7th Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure stated that at a blood pressure of 115/75mmHg cardiovascular disease risk doubles for each increment of 20/10mmHg throughout the blood pressure range (2).

Anti-hypertensive treatment is recommended (2-4) for individuals with a sustained systolic blood pressure of more than or equal to 160 mmHg or a sustained diastolic blood pressure of more than or equal to 100 mmHg. However, in the context of evaluating a potential living kidney donor additional issues need to be considered. Hypertension is known to be common following a nephrectomy (5,6) and in these circumstances a doctor is evaluating the potential future risk of hypertension in the donor and the associated potential long-term cardiovascular morbidity. It is important to note that even in the general population blood pressure will tend to rise naturally with age, and age and gender related threshold may be appropriate (7,8). In older donors a systolic blood pressure greater than the threshold of 140 may be considered acceptable.

Blood pressure measurement: large population surveys relating cardiovascular morbidity to blood pressure have relied on "office" blood pressure measurements. It is well known that some individuals have an alert reaction to the measurement of clinic blood pressure or so-called "white-coat hypertension" (9) and in this situation 24-hour ambulatory blood pressure monitoring (ABPM) may provide useful additional clinical information when assessing potential kidney donors (2-4,10). ABPM has been shown to correlate with hypertensive target organ damage (11) and is a better predictor of cardiovascular risk than office blood pressure (4, 12).

The British and European guidelines (3,4) define hypertension using ABPM as 24 hour mean blood pressure 125/80mmHg and the American guidelines (2) as awake blood pressure 135/85mmHg and asleep 120/75mmHg. Ozdemir et al (13) demonstrated that 24 hour ABPM was more sensitive at identifying hypertension in 71 potential renal donors than clinic blood pressure. In a study of 238 potential donors Textor et al (14) reported ABPM to be a useful technique to aid more accurate classification of hypertension (135/85mmHg) especially in older potential renal donors (>50 years) who tended to be misclassified as hypertensive more often. There is no specific evidence for the utility of self/home BP monitoring in potential kidney donors.

When considering a potential kidney donor the most difficult decisions relate to individuals who are found to have office readings above 140/90 mmHg but below the threshold for treatment with antihypertensive agents. If evidence of end

7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR

organ damage (hypertensive retinopathy or abnormal ECG, echocardiogram or chest X-ray), is present the potential donor is clearly hypertensive and kidney donation is contraindicated. If there is no evidence of end organ damage, repeated readings or 24-hour ambulatory readings may be of value. Kidney donation should be deferred if the readings exceed the thresholds quoted above. If, after treatment, the prospective donor is reconsidered, they fall into the category of the treated hypertensive patient. Potential donors with borderline hypertension should be warned of the possibility that uninephrectomy may accelerate the development of hypertension.

There is general agreement that kidney donation is contraindicated in those with hypertensive end organ damage, poorly controlled hypertension and hypertension that requires polytherapy to achieve adequate control. However, many units would be willing to accept a kidney donor with well-controlled hypertension and without any evidence of end organ damage. However, others would be reluctant to proceed on the basis that uninephrectomy may worsen the problem. Textor et al (15) demonstrated that in 58 donors with normal renal function and well controlled hypertension on 1or 2 anti-hypertensive agents (ACE inhibitor and a thiazide diuretic) that there was no increased risk to donor kidney function, microalbumin excretion or blood pressure control at 6 and 12months. However, this study does not address the issue of longer term safety and it cannot be assumed that the benign long term results of kidney donation associated with previous stricter criteria can be extended to these donors (15).

When considering what constitutes well-controlled hypertension in the context of kidney donation, a conservative approach should be adopted. The hypertension optimal treatment trial, which recruited 18,790 hypertensive patients, found that the incidence of major cardiovascular adverse events was lowest for those patients whose diastolic blood pressure on treatment was < 83 mmHg (16,17). The British Hypertension Society recently declared a systolic blood pressure of < 140 mmHg and a diastolic blood pressure of < 85 mmHg as optimal treatment targets (3).

When using ABPM mean daytime pressure to assess hypertension control the blood pressure would be expected to be 10/5 mmHg lower than office blood pressure target (3). The key issue when considering a prospective donor with adequately controlled hypertension is whether uninephrectomy has an adverse effect on subsequent control of blood pressure and therefore the total burden of cardiovascular risk. It is important to ensure measures have been taken to assess and minimise cardiovascular risk factors such as smoking cessation, cholesterol reduction etc if appropriate in prospective hypertensive donors.

In the past, individuals with hypertension and those on antihypertensive therapy have been commonly excluded as kidney donors and as a consequence there is relatively little information available. Torres et al (18) carried out a longitudinal study of blood pressure measurement in living kidney donors followed up for at least 10 years.

Ten of 66 kidney donors who were normotensive at the time of donation subsequently became hypertensive (defined as 160/95 mmHg) and of 24 donors most of whom had borderline hypertension before donation, 9 developed definite hypertension at follow-up. The authors suggested, on the basis of these observations, that donation of one kidney may accelerate the development of hypertension in patients with a predisposition to hypertension and suggested that individuals with borderline or treated hypertension should be advised not to donate. Torres et al (18) showed that after 10 years there is no increase in the occurrence of hypertension in donors but that blood pressure rises significantly in those with a predisposition to hypertension who had borderline hypertension at the time of donation At follow up of donors with borderline or definite hypertension 37.5% had hypertension compared with 15.2% of those with normal

7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR

blood pressure at the time of donation (18). Other single centre reports include very small numbers of hypertensive donors and it is difficult to interpret the data in a meaningful way. A large meta-analysis involving 3,124 patients after uninephrectomy (the majority being kidney donors) found an increase in both systolic and diastolic blood pressure of the order of 3 mmHg but no increase in the prevalence of hypertension (19).

Best Practice:

- *Prospective donors should not be precluded from further evaluation if their office (casual) blood pressure recordings are below 140/90 mmHg.*
- *Evidence of 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 (less than 140/85 mmHg (BHS). They should be warned of the possibility that nephrectomy may increase their blood pressure and subsequent cardiovascular risk and appro*priate follow *up should be arranged.*
- *Smoking, obesity and/or raised cholesterol in the context of hypertension place the donor at additional risk.*

7.10.3 Development of Hypertension Post Nephrectomy

There is no convincing evidence that unilateral nephrectomy significantly increases the risk of hypertension. The reported incidence of hypertension after kidney donation ranges from 9% in Turkey to 45% in the UK (6,22-26). Although these studies suggest that there is a high risk of developing hypertension after kidney donation they do not allow adequate assessment of any excess risk attributable to living renal donation, as the incidence of hypertension in the general population is not quoted.

Some small series from the USA have suggested an increase in hypertension after donation when adjusted to control groups (27- 29). However a recent large Swedish study of 402 donors with a mean duration since nephrectomy of 12 years showed that for females there was a lower prevalence of hypertension than in the age matched population with no difference for men. Goldfarb with a group of 70 donors with mean follow up duration of 25 years found no increased incidence of hypertension compared with the age matched general population. Two North American studies compared the incidence of hypertension in kidney donors with that in their siblings and found a difference in the (very high) incidence for hypertension between the groups (30,31). Furthermore, a meta- analysis of 48 studies involving 3,124 patient and 1,703 controls also concluded that uninephrectomy (the majority were organ donors) did not affect the prevalence of hypertension. There was however a small overall increase in blood pressure (19).

7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR

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7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR

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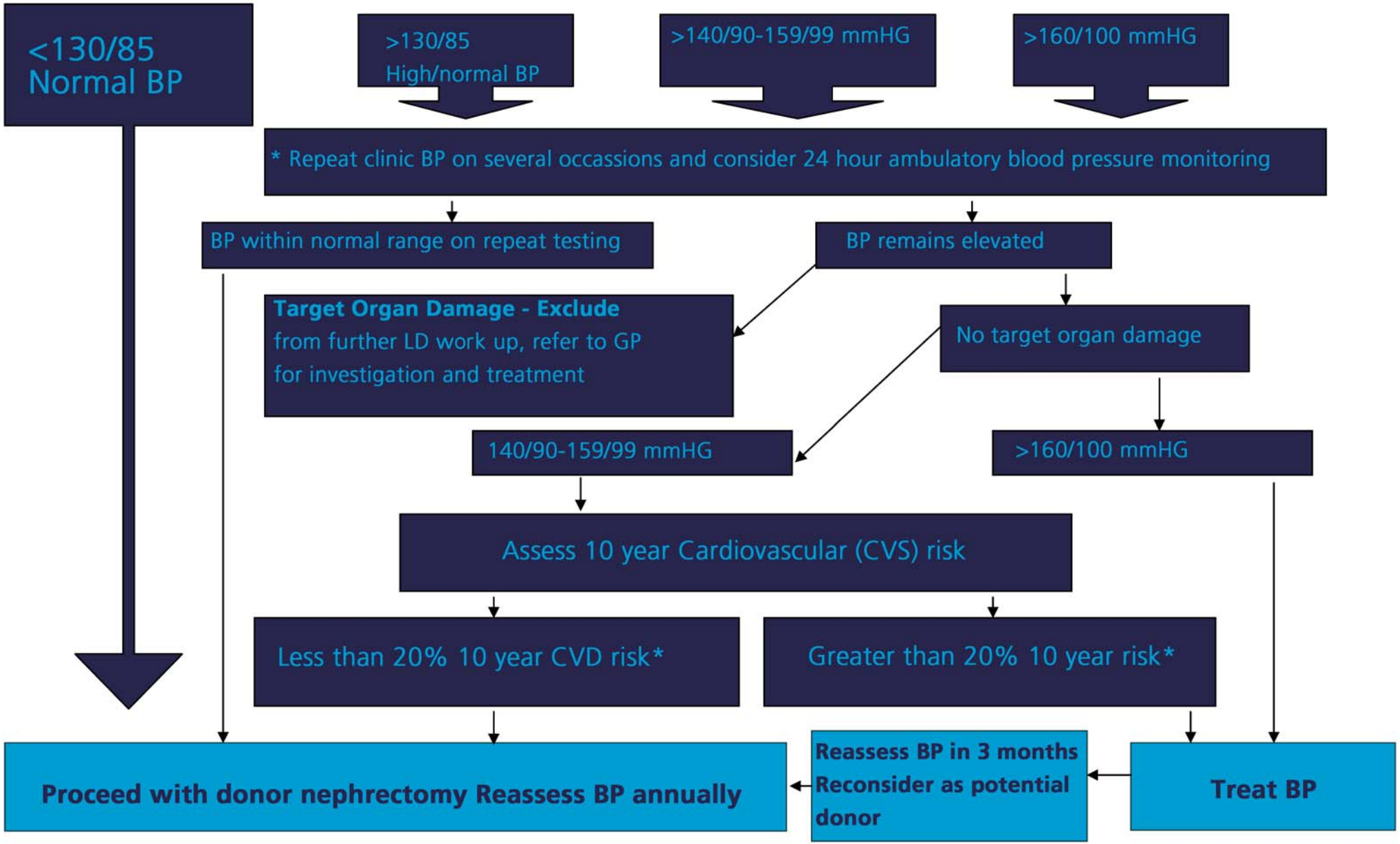
Assessment of blood pressure (BP) prior to living donor nephrectomy: Thresholds for intervention Initial BP (mmHg)

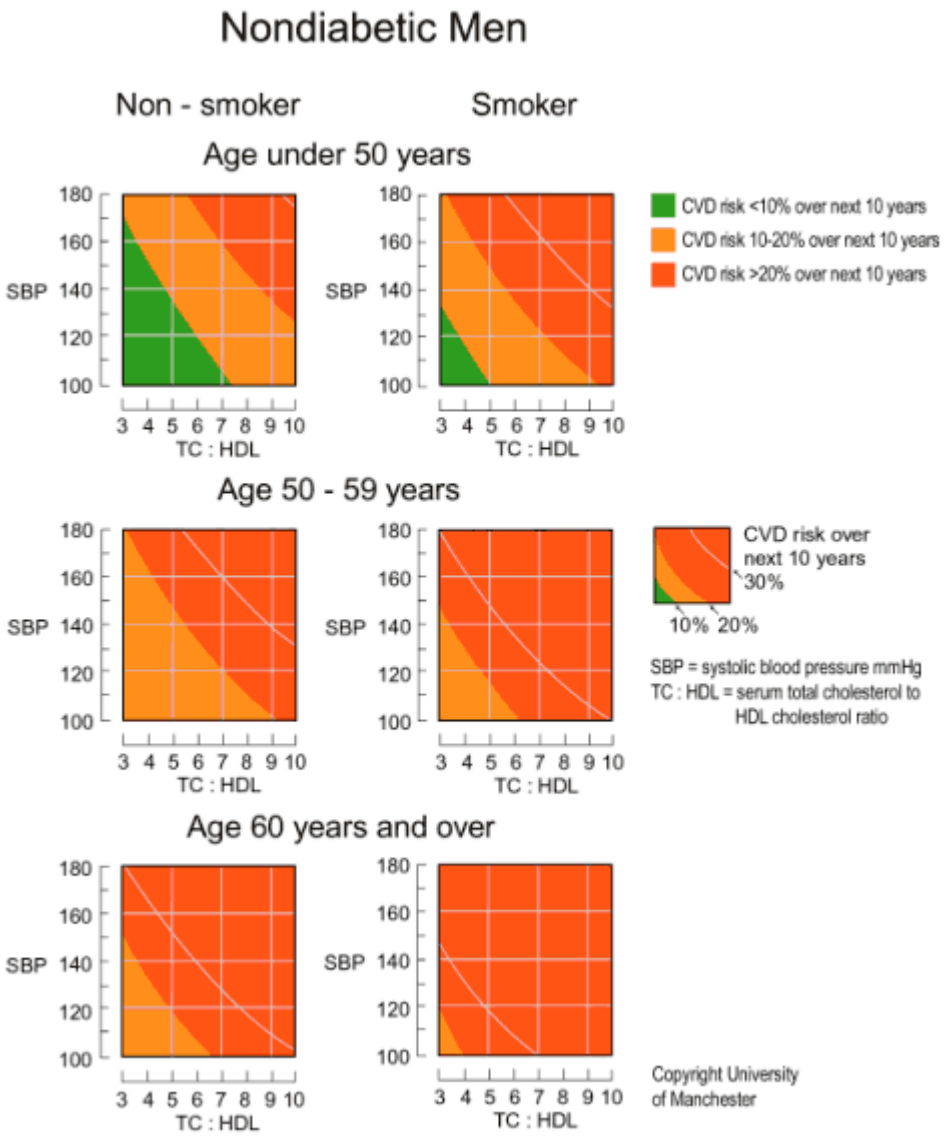
Figure 7.10.1
***Joint British Societies Cardiovascular disease risk prediction chart** - see below or www.hyp.ac.uk/bhs/resources/prediction_chart.htm



(BP - initial blood pressure (mmHg), CVD - cardiovascular disease)

7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR

Figure 7.10.2 - Joint British Societies Cardiovascular Disease Risk Prediction Chart



7.11 DONOR EVALUATION: DIABETES MELLITUS

7.11.1 Diagnosis of Diabetes Mellitus

To exclude diabetes mellitus, all prospective donors should have a fasting plasma glucose measurement. The WHO and American Diabetes Association recommend repeat testing of fasting glucose on a different day before placing someone in a glucose intolerance category (6). A fasting venous plasma glucose of > 7.0 mmol/l indicates diabetes mellitus and donation should not proceed (6). Fasting plasma glucose values of between 6.1 and 7 mmol/l indicate impaired fasting glucose. A glucose value in this range together with a family history of Type 2 diabetes mellitus (sibling or parental) is associated with a 30% 5 year risk of diabetes and donation is contraindicated (7). In the context of living donation, impaired fasting glucose is an indication for a standard 2-hour oral glucose tolerance test (OGTT). A 2-hour glucose value of > 11.1 mmol/l indicates diabetes (6). A value of > 7.8 mmol/l indicates impaired glucose tolerance. Caucasians in this latter category have a 10% 5 year risk of diabetes (7). The risk is higher for certain ethnic groups, notably individuals from Southern Asia and the Caribbean (8). Testing for glycosuria and measurement of random glucose levels has low sensitivity in the diagnosis of diabetes (9). After exclusion of pre-existing diabetes, the clinical risk factors for diabetes and diabetic nephropathy should be evaluated and discussed with the potential donor (3, 4).

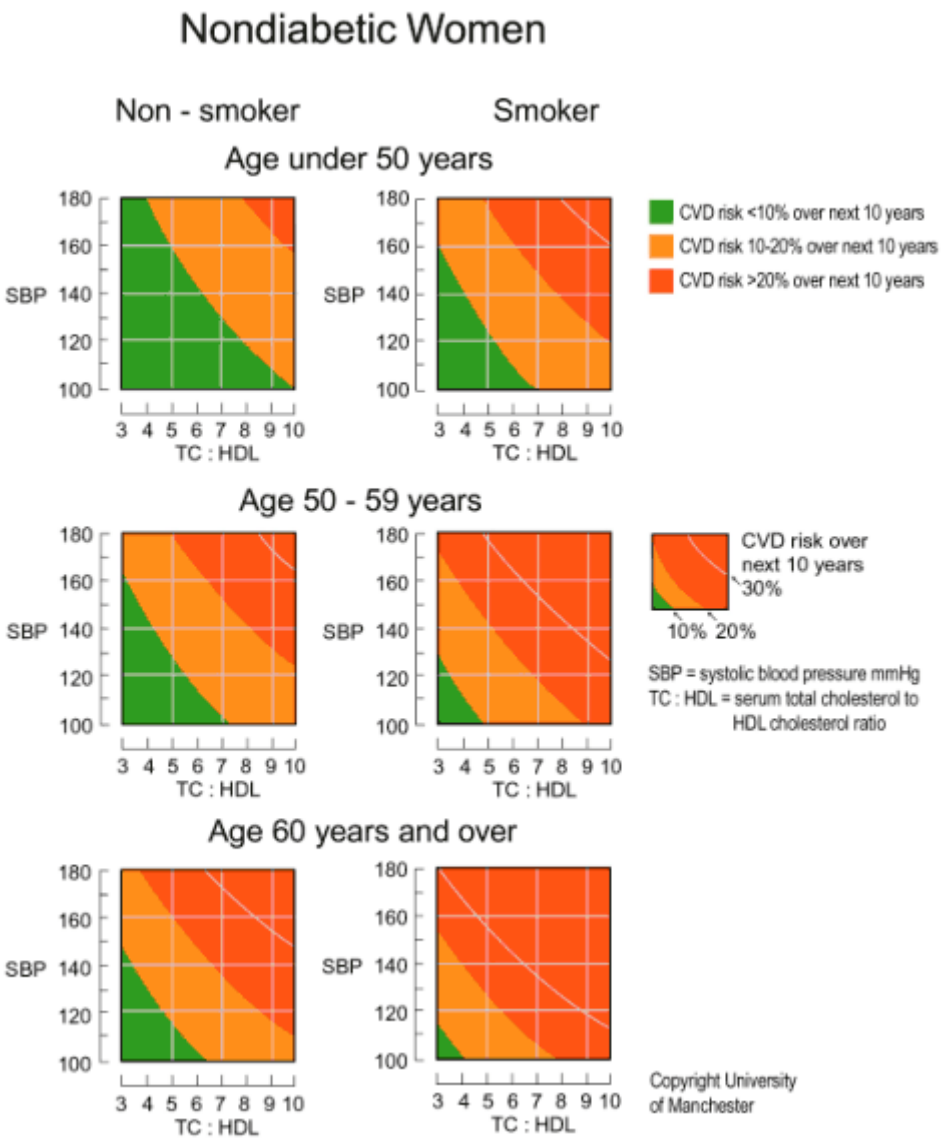
7.11.2 Risk of Type 1 Diabetes

Type 1 diabetes presents predominantly in childhood and early adulthood and 50% of cases have presented by the age of 20 years (10). The incidence of Type 1 diabetes in adults is less than 1 in 10,000 (10). First degree relatives of an individual with Type 1 diabetes have a 15 fold increased risk of developing the disease. Moreover, the relatives of Type 1 diabetics with diabetic nephropathy appear to be at increased risk of nephropathy should they subsequently develop diabetes (11). However, because Type 1 diabetes is relatively uncommon and most cases have presented before the age at which living donation is under consideration, there is little need for concern even when there is a family history of Type 1 diabetes. Sometimes it may be difficult to determine from the history whether an affected family member had Type 1 or Type 2 diabetes. As a working definition, Type 1 diabetes mellitus is characterised by onset below the age of 30 years and requirement for insulin treatment from the time of diagnosis.

7.11.3 Risk of Type 2 Diabetes

Type 2 diabetes mellitus is predominantly a disease of later life and in 50% of cases Type 2 diabetes is clinically unrecognized (12). The crude prevalence of undiagnosed disease in the Caucasian population is 2.3% (13). Individuals who have a family history (first degree relative) of Type 2 diabetes mellitus are at higher risk of developing the disease (relative risk 3.0). Because the prevalence of Type 2 diabetes mellitus is much higher than for Type 1, the absolute risk of developing the disease is high (life time risk 38%) (14). The combination of family history and obesity (BMI > 30) places an individual at very high risk of diabetes in later life (15). Individuals from South East Asia and the Caribbean are at increased risk of Type 2 diabetes mellitus, independent of age and obesity. Individuals at high risk of Type 2 diabetes because of a positive family history and/or obesity should undergo an OGTT and should only be considered further as donors if this is normal. For individuals with a normal OGTT, the risk of developing Type 2 diabetes mellitus within 5 years is around 1% overall and is modulated by ethnicity and obesity. If there is a history of transient gestational diabetes, the risk of Type 2 diabetes is very high (16, 17) and kidney donation is not advised. An important consideration for a potential kidney donor is the risk of developing nephropathy should they subsequently develop Type 2 diabetes. There is a sharp increase in the incidence of Type 2 diabetes after the age of 50 and the median age at diagnosis is around 60 years. Less than 1% of Europeans with Type 2 diabetes mellitus develop ESRD but the incidence is higher in other ethnic groups (18). However, there is a 50% cumulative incidence of proteinuria after Type 2 diabetes mellitus has been present for 20 years (19) which may reasonably become an issue for kidney donors who have an above average life expectancy and may expect to live

7.10 DONOR EVALUATION:HYPERTENSION IN THE DONOR



Cardiovascular Disease Risk Prediction Chart reproduced with permission from The University of Manchester Department of Medical Illustration, Manchester Infirmary

7.11 DONOR EVALUATION: DIABETES MELLITUS

to their 80s (20). A prudent approach should be adopted when assessing potential donors who are at increased risk of Type 2 diabetes mellitus.

Best Practice:
Diabetes mellitus is an absolute contraindication to living donation. Prospective donors with an increased risk of Type 2 diabetes mellitus because of family history, ethnicity or obesity should undergo a glucose tolerance test and only be considered further as donors if this is normal.

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7.12/13 DONOR EVALUATION: PROTEINURIA & PYURIA

7.12 PROTEINURIA

The presence of proteinuria is a strong independent predictor of future end stage renal disease in the general population (1). Even a slight increase in proteinuria was found to be a risk factor for this (dipstick positive proteinuria - odds ratio was 2.71) and always warrants further investigation. Previous studies have shown that some but not all patients develop proteinuria and hypertension following uninephrectomy (2-4). Goldfarb et al (5) reported that proteinuria increased with marginal significance (19% had 24 hour protein excretion of >0.15g/24 hrs and 7% >0.8g/24hrs) in 70 renal donors after a mean of 25 years follow up. They concluded that borderline proteinuria before donation identified a group at risk for the development of significant proteinuria 25 years after donation. Studies in the general population have shown that smoking, obesity, hypertension and elevated blood glucose levels are associated with an increased risk of proteinuria (6, 7) and recently, authors have suggested that other factors may be important in the development of proteinuria following nephrectomy. In a study of 73 patients, Praga et al (8) reported that 13 out of 14 (92%) obese patients (BMI >30) developed proteinuria and renal impairment after mean follow up of 10 years compared to 12% non-obese donors.

Tozawa et al (6) showed smoking and obesity impact upon renal function, blood pressure and cardiovascular risk. In this study the number of cigarettes smoked per day was associated with increased risk of proteinuria with a relative risk of 1.4 (p=0.08). Similarly, Brigitani et al (9) reported smoking to increase risk of proteinuria in men in the general population (RR 3.59. They also reported an association between the pack years smoked and GFR - GFR decreased 3.2ml/min/1.73m2 for every 10 pack years smoked in men particularly (9). Therefore, informed consent of the living donor includes a discussion of lifestyle risk. The impact of cumulative cardiovascular risk factors should be discussed with the donor.

7.12.1 Screening for Proteinuria in Prospective Donors

Urine protein excretion should be estimated in all prospective living donors. A number of methods can be used to quantify proteinuria. Dipstick testing of the urine is a useful screening test, but is only semi-quantitative and not by itself sufficient. A correctly performed 24hour urine collection provides the most accurate assessment, but incomplete collection can underestimate any protein leak. Up to 150 mg of protein per 24 hours is usually considered normal (10,11). A urine protein (mg/dl) to creatinine (mg/dl) ratio of less than 0.2 will usually exclude significant proteinuria without the need for a timed urine collection (12). Orthostatic proteinuria only occurs in the upright position and is seen most often in young males. Proteinuria is not present in early morning urine samples collected after resting supine and the 24hour protein excretion does not usually exceed 1g. The pathogenesis of the condition is unclear but in virtually all cases it is benign (13-15) and is *not usually* considered to be a contraindication to kidney donation but maybe in some units. It is, however, essential to be confident of the diagnosis before proceeding since other causes of proteinuria commonly show a degree of postural variation early in their course. On rare occasions serious glomerular disease may develop in patients with orthostatic proteinuria (16). Transient proteinuria sometimes occurs in response to exercise or fever. Proteinuria may occasionally be of tubular origin and may be due to tubular damage from exogenous toxins, myeloma or amyloidosis which would preclude kidney donation.

Best Practice:
Urine protein excretion should be quantified by analysis of a 24hour urine collection or spot urine protein: creatinine ratio. Increased urine protein excretion usually excludes further consideration as a kidney donor.

7.12/13 DONOR EVALUATION: PROTEINURIA & PYURIA

7.12.2 Post Nephrectomy Proteinuria

Asymptomatic proteinuria is common after unilateral nephrectomy. A small increase in proteinuria has been reported in up to a third of kidney donors (2, 4,18-25). However, the level of proteinuria is generally mild (less than 0.5 gm/24 hr), is not progressive and has no adverse effects on the health of the donor. The development of proteinuria post nephrectomy has recently been related to obesity in the individual at the time of nephrectomy in one series. Goldfarb et al found 90% of subjects had a 24 hr urinary protein excretion of greater than 0.5 mg. The mean urinary protein excretion rose from 0.08gm/24 hr prior to nephrectomy to 0.23gm/24 hr post nephrectomy.

7.13 PYURIA

The presence of white cells in the urine at a concentration exceeding the normal limits appropriate to gender may indicate transient urinary tract infection or underlying renal parenchymal disease (11,17). The cause of the pyuria must be established before a potential donor proceeds for further assessment.

Best Practice:
Prospective donors found to have pyuria should only be considered further for donation if it can be demonstrated that it is due to a reversible cause, such as an uncomplicated urinary tract infection.

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7.12/13 DONOR EVALUATION: PROTEINURIA & PYURIA

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7.14 DONOR EVALUATION: MICROSCOPIC HAEMATURIA

Microscopic haematuria in a previously asymptomatic individual is an increasingly common issue in the investigation of living kidney donors. Standard reagent strips frequently produce false positive but rarely false negative results (1,2). It is recommended that a minimum of two dipstick urine tests are performed on separate occasions during the course of the donor assessment to exclude the possibility of intermittent microscopic haematuria. If the initial reagent strip test is positive for blood, in the absence of any obvious cause such as infection and/or menstruation, the test should be repeated on three further occasions, several days apart. If these subsequent tests are negative, there is no cause for concern. If two or more tests are positive under these circumstances, it is indicative of a persistent problem, which requires full investigation (see table 7.14.1).

Table 7.14.1 - Investigation of asymptomatic microscopic haematuria in the potential living donor

Persistent asymptomatic microscopic haematuria defined by

two or more positive dipstick urine tests on separate occasions

↓

Perform **urine culture** and **cytology**, **cystoscopy** and **renal imaging** to exclude common urological causes e.g.; persistent infection, nephrolithiasis and urothelial carcinoma

↓

In the absence of a urological cause, **renal biopsy** must be performed

General population studies provide some information about the incidence of microscopic haematuria in the normal population. A three month home-screening study of men of 50 years of age and over showed a 10% incidence of microscopic haematuria on at least one occasion (3).

A cumulative study of male soldiers with annual urine testing over a 12 year period showed an incidence of 39% of microscopic haematuria on at least one occasion, with 16% having two or more positive tests (4). A 13% incidence of transient microscopic haematuria has been reported in post-menopausal women (5). The dipstick test is the most reliable test. Examination of fresh, centrifuged urine sediment for the presence of red cells and cellular casts which indicate glomerular bleeding can be helpful (6). Routine MSUs without centrifugation will not be reliable to exclude haematuria.

Renal Biopsy

There are a number of histological diagnoses which may be made. Glomerular causes include IgA nephropathy, thin basement membrane nephropathy and hereditary nephritis (4, 5, 7-10). Mesangial proliferative glomerulonephritis, IgA positive, is a contraindication to donation.

In mesangial proliferative glomerulonephritis, IgA negative, there is no consensus as to the risks involved. There is uncertainty over the nature of thin membrane disease and its relationship to genetic abnormalities in Type IV collagen and Alport's syndrome (11). It is suggested in such cases that advice from a clinical geneticist is sought.

Best Practice:
Persistent microscopic haematuria in the potential living donor requires full investigation to identify an underlying cause, up to and including renal biopsy if there is no obvious urological explanation. Where there is insufficient evidence to quantify the risks following histological diagnoses of renal pathology, donation is not recommended. Advice from a clinical geneticist is recommended when a diagnosis of thin membrane disease is made as new data is being generated all the time.

7.14 DONOR EVALUATION: MICROSCOPIC HAEMATURIA

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7.15 DONOR EVALUATION: NEPHROLITHIASIS

Nephrolithiasis is a relative contraindication to kidney donation because the donor is at risk of further stone disease. The prevalence of nephrolithiasis in the UK is around 3-5% and the incidence of symptomatic stone disease is about 0.5% per year (2). Patients who have passed a stone are significantly more likely to pass additional stones (2) and up to 50% of patients with a calcium stone will pass another stone within 5 years (3, 4). Biochemical assessment should be undertaken in prospective donors with a history of urinary stones or, if there are risk factors for stone disease, specialist advice should be obtained. The metabolic risk factors for stone formation include hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitraturia. Investigations should include plasma calcium and uric acid levels, together with 24hour collection for estimation of calcium, oxalate, uric acid, citrate and cystine (12, 13). Although there is not evidence to support it, in practice a stone in the renal parenchyma of < 5mm would not be considered a contra-indication to donation.

If there is a history of stone disease, plain abdominal X-rays and intravenous urography are necessary, to exclude current stones or anatomical abnormalities that may be the cause or result of previous stone formation. Spiral CT scan is the most sensitive investigation for stone detection (14). If a potential donor has passed a single stone more than ten years previously it may be acceptable to proceed to living donor nephrectomy if a metabolic tendency to stone formation has been excluded (11). Calcium oxalate stones account for around 80% of all stones and many cases are associated with varying degrees of idiopathic hypercalciuria (8, 9, 10). Struvite stones are associated with infection by urea splitting organisms. They represent around 15% of all stones (8, 9) and are usually considered an absolute contraindication to donation. The composition of a stone may help to identify a predisposing cause (5, 6, 7). Cystine, uric acid and calcium phosphate stones (8, 9) account for 2-5% of stones and usually preclude kidney donation. Inadvertent transplantation of a kidney containing a stone may also harm the recipient although this is uncommon (1).

7.15.1 Long Term

There are no firm data for the outcome of individuals with previous renal stone disease who have donated a kidney. Modern advances in the management of nephrolithiasis may make the occurrence of a stone in a single kidney a less important issue where sophisticated services are available within the health care system to deal with this eventuality. It is unclear what the implications are for a donor who has never passed a kidney stone but is found to have one during the donor assessment process.

If a patient with a history of stone disease is, after full assessment, accepted as a kidney donor, life long follow-up is important to allow early detection of urinary sepsis, metabolic abnormalities or recurrent stone formation. Both donor and recipient should be informed about the small but unquantifiable risk to the remaining kidney in the donor and (possibly) to the transplanted kidney. The need for fully informed consent is paramount and, if donation proceeds, it may be advisable to use the kidney from which the stone was previously passed for transplantation. The donor should be advised of the importance of ensuring a good fluid intake to reduce the risk of further stones. Particular caution should be exercised when potential donors from overseas are evaluated in this context, with consideration given to future follow-up arrangements in their country of origin. Such donors may be at increased risk of future stone disease.

7.15 DONOR EVALUATION: NEPHROLITHIASIS

Best Practice:
There is poor evidence to support an unequivocal position with regard to renal stone disease. A history of nephrolithiasis is not an absolute contraindication to donation. In the absence of a predisposing metabolic condition, it would seem prudent to proceed if the disease has been inactive for ten years. In individuals who are found to have renal stones during donor assessment, without a history of passage and no predisposing metabolic condition, the lack of data will need to be shared with the patient. If, after full assessment, a patient with a history of stone disease is accepted as a donor, life long follow-up is essential to allow early detection of urinary sepsis, metabolic abnormalities or recurrent stone formation.

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7.16 DONOR EVALUATION: INHERITED RENAL DISEASE

When renal failure in the recipient is due to an inherited renal disease or there is a family history of renal disease the emphasis is on thorough investigation of any genetically related potential donor (1). The genetic basis of a number of syndromes has become clear in the past few years (2). In some specific cases DNA analysis can indicate whether the potential donor has the condition, but in others a large kindred may be needed to determine this on genetic analysis. Some syndromes have clinical manifestations, which inform the donor assessment process. In autosomal recessive or sex-linked conditions the potential donor may carry a gene but will not develop the same clinical features as the potential recipient. In this instance, analysis of risk to the potential donor is more important than whether he/she has inherited a specific gene. The genetic information on many of these syndromes is expanding rapidly (2) and it would be unreasonable to expect the donor assessment team to be aware of its totality. The involvement of a clinical genetics department and case conference with the donor, recipient (+/- other family members) and the donor assessment team may be required.

Some conditions in which renal dysfunction may be inherited include:

- Autosomal dominant adult polycystic kidney disease (ADPKD)
- Autosomal recessive juvenile polycystic kidney disease
- Alport's syndrome
- Congenital nephrotic syndrome
- Vesico-ureteric reflux
- Von Hippel-Lindau disease
- Familial juvenile hyperuricaemic nephropathy
- Anderson-Fabry disease
- Familial Haemolytic Uraemic syndrome
- Dent's Disease
- Familial FSGS

In the majority of these conditions the presence of the disease in the donor precludes transplantation. The most common inherited renal disease is ADPKD, affecting 1:1000 individuals (2). Diagnosis of ADPKD is based on the following radiological criteria:

- At least two cysts unilaterally or bilateral single cysts in individuals aged < 30 years.
- At least two cysts in each kidney for individuals aged 30 to 59 years.
- At least four cysts in each kidney for individuals aged > 60 years.

A negative renal ultrasound beyond the age of 30 years virtually (98% sensitivity) excludes ADPKD. Between the ages of 20-30 years a negative ultrasound should be followed by a CT scan.

Alport's syndrome is an example of where the involvement of a clinical geneticist should be sought. This is most commonly inherited as an X linked disorder of type IV collagen (2). The average age of ESRF in males is 21 years. The clinical course in female carriers is extremely variable. A few are as severely affected as males, but the majority are clinically asymptomatic throughout a normal lifespan. Overall, about 15% of female carriers develop ESRF. Consideration of the use of female heterozygotes of Alport's, who have microscopic haematuria but otherwise normal renal function should involve consultation between the donor assessment team and clinical geneticists.

Vesico-ureteric reflux is a condition where the clinical features are indicative but the genetic basis is unclear (2). It affects around 1% of infants and is one of the most common reasons for transplantation in young adults. A careful search for evidence of reflux or its consequences should be undertaken in genetic relatives being considered as donors. A history of enuresis or urinary infections as a child is common in affected individuals. Nuclear medicine scanning can detect renal scars and this can be used to look for indirect evidence of reflux in potential donors.

7.16 DONOR EVALUATION: INHERITED RENAL DISEASE

Best Practice:
When the cause of renal failure in the potential recipient is due to an inherited condition other than Adult Polycystic Kidney Disease, it is appropriate to consult a clinical geneticist if a genetic relative is considered as a potential donor.

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7.17 DONOR EVALUATION: DONOR MALIGNANCY

The accidental transmission of malignant disease from donor (deceased or living) to recipient by kidney transplantation is well described (1). To minimise this risk, care must be taken during evaluation of the donor to ensure that there is no past medical history of malignant disease or symptoms consistent with undiagnosed malignancy. During clinical examination, the possibility of occult malignancy should be borne in mind and care taken to exclude the presence of abdominal masses, breast lumps, testicular swelling and lymphadenopathy. Unless there is concern on the basis of history, clinical examination or routine investigations, it is not necessary to screen for tumour markers (e.g. PSA, CEA, and alpha- fetoprotein).

If the potential donor gives a history of treated malignant disease there are no reliable data from which to accurately predict the risk of tumour transmission to the recipient. The situation is further complicated by wide variations in the natural history of different primary tumours. There is universal agreement that tumours with a propensity to late recurrence, for example breast cancer, malignant melanoma and sarcomas are an absolute contraindication to organ donation, irrespective of the tumour free interval. For other types of malignancy, it has been suggested that consideration for donation may be appropriate if there is no evidence of tumour recurrence after ten years (2). Factors such as the natural history of the disease, the grade, stage and site of the tumour and the disease-free interval must all be taken into account when assessing the risk of transmission.

A tumour free interval of less than five years would rarely be considered acceptable and for many types of primary malignant tumours donation should probably be excluded irrespective of the follow-up period. Documentation submitted to the Council of Europe on this issue recommends that organs and tissues from donors with a history of neoplastic disease should not normally be used. If, however, a donor is considered to be suitable in principle, further assessment should include appropriate tests to exclude evidence of local recurrence or distant spread of the original tumour.

Previously treated low-grade non-melanotic skin cancer and carcinoma *in situ* of the uterine cervix are not usually considered as contraindications to kidney donation.

Best Practice:
Malignant disease is a contraindication to living donation, and the same standards should be adopted as for deceased donors. Apart from low-grade non-melanoma skin cancer and carcinoma in situ of the uterine cervix, previously treated malignancy usually excludes further consideration as a kidney donor.

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7.18 DONOR EVALUATION: ANGIOMYOLIPOMATA

Angiomyolipomata are rare, benign neoplasms composed of mature adipose tissue, smooth muscle and thick walled blood vessels. With modern imaging techniques the diagnosis as well as the discrimination from the uncommon subtype of epitheloid angiomyolipoma, which may not have a benign phenotype, can usually be made without requiring biopsy.

The largest single series observing the natural history of isolated angiomyolipomata (not as part of Tuberous Sclerosis complex) comprises 29 patients followed for approximately four years (1). Four patients had bilateral tumours. A large proportion (40%) presented with symptoms; pain, a mass, haemorrhage or haematuria. This group would be predicted to have a more adverse outcome compared to those discovered as part of living donor work up. The initial mean tumour size was 4.5 cm and at an average follow up of 4 years (range 1 to 14 years) 21% of tumours grew. Overall, the proportion of tumours that grew was double if the tumours were more than 4 cm in diameter at presentation.

For living donors, bilateral disease would preclude donation. In unilateral disease, only the affected kidney should be considered for donation. If the tumour is 4 cm or larger, donation should only be contemplated if *ex vivo* excision of the tumour is possible, because of the risk of subsequent symptoms. This approach has been published as case reports (2,3). If the tumour is small, for example 1 cm or less and its position makes *ex vivo* removal particularly difficult, then donation followed by bi-annual ultrasound surveillance is reasonable and has also been published as a case report (4). For tumours between 1cm and < 4cm in diameter there is little evidence available and management will depend, in part, on the position of the tumour.

Best Practice:
Bilateral angiomyolipomata preclude living renal donation. Kidneys containing lesions of:
4cm or larger should only be transplanted if ex vivo excision of the tumour is straightforward.
1cm or smaller may be transplanted and followed with serial ultrasound imaging.
Between 1cm and 4cm in diameter need to be assessed on a case-by-case basis and the lack of evidence shared with the donor and recipient pair.

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7.19 DONOR EVALUATION: INFECTION IN THE PROSPECTIVE DONOR

The risk of transmission of infections between donor and recipient must be kept to a minimum. The same principles that apply to deceased donors and blood donors in this respect should be applied to the screening of living donors (1, 2). Identification of current or previous infection in the prospective donor is an important aspect of donor evaluation. The presence of active infection usually precludes donation. Apart from the implications for the potential donor, a number of infections may be transmitted by organ transplantation. Those that are of established clinical significance are listed in the following tables.

Table 7.19.1

Viral infections of established clinical significance

Human immunodeficiency virus (HIV-1 and HIV-2)
Human T lymphotrophic virus (HTLV)
Hepatitis C virus (HCV)
Hepatitis B virus (HBV)
Cytomegalovirus (CMV or HHV 5)
Herpes simplex virus (HSV or HHV1 and HHV2)
Varicella-zoster virus (VZV or HHV3)
Epstein-Barr virus (EBV or HHV4)
Kaposi's Sarcoma virus (KSKV or HHV8)

Table 7.19.2

Bacterial, fungal and parasitic infections of established clinical significance

Bacterial

Bacterial meningitis
Mycobacterium tuberculosis (MTB)
Atypical mycobacterial infections
Syphilis*

Fungal and parasitic

Malaria
Toxoplasmosis
Schistosomiasis

*Transmission of syphilis is a theoretical risk. No case has yet been reported related to organ transplantation, but several have been reported following blood transfusion. Other infections are either rarely transmitted (occasional case reports) or of theoretical risk only.

Table 7.19.3

Prion-associated diseases of established clinical significance

Creutzfeld-Jakob disease (CJD) and variant CJD (vCJD)

7.19.1 Evaluation of the Prospective Donor

A detailed clinical history is important and should include a psychosocial and sexual history to define at-risk behaviour, (see Table 7.2 in Section 7.3). Prospective donors who have been resident in geographical areas outside the UK where there is a high prevalence of infection may require additional evaluation. During routine physical examination of the donor, examination of the chest and reticuloendothelial system may reveal evidence of infection. The routine screening investigations already outlined in Table 7.4 in Section 7.3 include those ordinarily required to exclude infection in the prospective donor. Particular attention should be paid to the possibility of past tuberculosis when examining the chest X-ray.

7.19 DONOR EVALUATION: INFECTION IN THE PROSPECTIVE DONOR

A mid-stream urine should be cultured and examined by microscopy on several occasions. If sterile pyuria is detected the cause must be identified. The presence of eosinophilia may indicate chronic parasite infection.

The serological tests that should be performed on the prospective donor and recipient are listed in Table 7.19.3. Infections can be transmitted by both blood transfusion and organ donation during the incubation period of the offending organism and before a serological response has been mounted. Serology should not, therefore, be regarded as a substitute for a detailed psychosexual and medical history. Routine testing for viral infection may, if a positive result is obtained, raise complex ethical problems. It is important that there is full discussion with the prospective donor before testing for viral infection, particularly for human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV). A strategy for dealing with a positive result should be formulated before testing.

7.19.2 Viral Infections in the Prospective Donor

HIV and HTLV

The presence of HIV or human T lymphotrophic virus (HTLV) infection is an absolute contraindication to living donation. HTLV serology is not routinely tested but should be performed if the prospective donor comes from an endemic area e.g. Africa, the Caribbean and Japan. Kidney donation should not be undertaken if significant doubt remains about the possibility of HIV infection in the donor.

HCV

HCV is a relatively strong contraindication to living donation not only because of the risk of transmitting HCV to the recipient but also because of the risk of glomerular disease in the donor (3, 4). The risk of HCV transmission from an HCV positive donor approaches 100% (5). All potential donors should have HCV antibody testing performed and if positive, HCV RNA should be checked. In the exceptional circumstance of transplanting a kidney from an HCV-positive donor, the likely life expectancy of the recipient has to be considered as well as their pre-transplant HCV status.

If transplantation is being considered from an HCV-positive donor, the risks must be carefully explained to the donor and recipient. Advances in anti-viral agents and vaccination may influence such decisions in the future.

HBV

Most transplant units regard HBV infection in the donor as an absolute contraindication to transplantation. All prospective donors should have both HB surface antigen and HB core antibody IgG checked. HBV DNA testing should be performed in prospective donors from HBV endemic areas who are hepatitis core antibody positive, those with possible mutant HBV and those with abnormal liver tests or a past history of liver disease of unknown aetiology. HB core antibody IgM is not indicated unless the donor is e antigen positive and acute infection is being queried.

There are occasional reports of kidneys transplanted from HB surface antigen negative, HB core antibody-positive deceased donors with a low risk of HBV seroconversion and no excess risk of graft failure or short-term morbidity (6,7). For recipients of a kidney from an HBV positive donor, a combination of vaccination, HBV immunoglobulin and anti-viral drugs could be considered. Advice from a virologist should be sought under these circumstances.

Summary point:
HCV and HBV infection in the donor are usually a contraindication to living donor kidney transplantation.

CMV

CMV infection is the most commonly encountered clinically significant viral infection after kidney transplantation (8) and may cause significant morbidity and mortality, particularly if the recipient is heavily immunosuppressed. It also increases the risk of chronic graft dysfunction as well as post-transplant lymphoproliferative disorder (PTLD) and opportunistic infection.

7.19 DONOR EVALUATION: INFECTION IN THE PROSPECTIVE DONOR

CMV disease may result from reactivation of latent infection or because of primary infection transmitted by a kidney from a CMV positive donor. For CMV, and other viral infections, primary infection is generally more severe than reactivation and recipients most at risk are those who are CMV-seronegative and receive a kidney graft from a CMV-seropositive donor. Matching CMV seronegative recipients with CMV-seronegative donors is an effective strategy for reducing the risk of CMV infection but is not practicable in the context of living donor kidney transplantation. CMV prophylaxis and pre-emptive therapy with close monitoring should be offered (9). The donor and recipient should be informed before the transplant is performed about the increased risk of CMV disease.

Best Practice:
The CMV status of donor and recipient should be determined before transplantation. CMV-seronegative recipients of a kidney from a seropositive donor should be warned of the increased risk of CMV infection and be managed according to BTS Guidelines (9).

EBV
Primary EBV infection is most likely to occur in EBV negative paediatric recipients who receive a kidney from an EBV-positive donor. EBV infection increases the risk of PTLD several fold and this risk is increased further if the recipient is given antilymphocyte antibody immunosuppressive therapy. Consideration should be given in this situation to the prophylactic use of antiviral agents (acyclovir or gancylovir) in order to minimise the viral load after transplantation. This strategy may protect renal transplant recipients from PTLD (10), but is not of benefit in paediatric liver transplant recipients (11). When the donor is EBV-positive and the recipient is EBV negative clinical vigilance is required following transplantation to detect PTLD as early as possible. Monitoring the recipient with quantitative PCR for viral load is contentious.

VZV
It is important to know whether the potential recipient is VZV seropositive or not as a primary VZV infection may be rapidly fatal in an immunocompromised host. (12,13) Vaccination is available for VZV antibody negative recipients.

HHV8
HHV8 may be transmitted by organ transplantation and is associated with an increased risk of Kaposi's sarcoma (14).

7.19.3 Bacterial Infections in the Prospective Donor

The main risk of bacterial infection is from Mycobacterium tuberculosis (and atypical Mycobacteria). Donors should be screened for mycobacterial infection. This will include a careful history, including ethnic origin and country of upbringing. Chest X-ray is important but the value of skin testing is questionable. If a specific bacterial microbiological diagnosis has been made in the donor, then a course of appropriate antibiotic is likely to be effective in preventing transmission (Table 7.19.4).
A history of urinary tract infection in a potential donor, particularly if there is a family history of reflux nephropathy or, in a male, requires detailed imaging of the kidneys (e.g. DMSA for cortical scarring (See section 7.4).

7.19 DONOR EVALUATION: INFECTION IN THE PROSPECTIVE DONOR

7.19.4 Fungal and Parasitic Infections in the Prospective Donor

A living donor is unlikely to transmit a fungal infection if otherwise in good health. Nevertheless this remains a theoretical possibility and should be considered in patients from areas where fungal infections are endemic. Toxoplasmosis and malaria can be transmitted by a renal transplant (12).

In most of the reported cases, transmission has been from living unrelated donor transplantation taking place in the developing world.

Other infections are either transmitted rarely (occasional case report) or of theoretical risk, for example prior related diseases. Table 7.19.4 summarises the use of prophylactic antimicrobial agents for different types of donor infection.

Table 7.19.4 Serological testing of donor and recipient

Donor screening	**Recipient screening**
HIV 1 & 2	HIV 1 & 2
CMV	CMV
VZV	
EBV	EBV
HCV	HCV
HBV	HBV
Syphilis	
Toxoplasmosis	
*HHV8	*HHV8
*HTLV	*HTLV
*Schistosomiasis	*Schistosomiasis
*Strongyloides Stercoralis	*Strongyloides Stercoralis
*Malaria (blood film)	*Malaria (blood film)
*Trypanosoma cruzi	*Trypanosoma cruzi

*Where clinically indicated e.g. specific endemic (geographical) risks

7.19 DONOR EVALUATION: INFECTION IN THE PROSPECTIVE DONOR

7.19.5 Prion-Associated Diseases in the Prospective Donor

CJD and vCJD

There is no screening test currently available for CJD or vCJD. National guidance for blood and tissue donors states that prion-associated disease in the prospective donor is an absolute contra-indication to donation (2). Individuals who may be at increased risk of developing such a disease are also precluded from donating and a detailed personal and family history must be taken from the donor to identify potential risk factors. Healthy living donors may not have been exposed to many of these but relevant history would include recipients of human pituitary-derived (growth) hormones, dura mater, corneal and scleral grafts and a positive family history (two or more blood relatives) of prion-associated disease, subject to genetic counselling. If a prospective donor has received a transfusion with blood or blood products within the British Isles since 1st January 1980, or received autologous blood within 12 months prior to the potential donation, he/she is precluded from donating. The 12 month rule also applies to recipients of transfusions of blood or blood products in Western Europe, North America, Australia and New Zealand. Separate specialist advice should be sought for donors who have received transfusions in other countries (2).

Table 7.19.5 Use of prophylactic antimicrobial agents

1	HBV positive donor		Vaccinate recipient HBV Immunoglobulin
2	CMV (donor +ve, recipient –ve)		Phrophylactic antiviral drugs indicated
3	EBV (donor +ve, recipient –ve)		Consider phrophylactic Acyclovir Or Gancyclovir
4	Toxoplasmosis		Sulphonamide, Clindamycin, Clarithromycin, Azithromycin Or pyrimethamine
5	Mycobacterial infections		Prophylactic Isoniazid
6	Bacteria	Low virulence High virulence	7 days of appropriate antibiotic 14 days of appropriate antibiotic
7	Syphilis		Benzylpenicillin

7.19 DONOR EVALUATION: INFECTION IN THE PROSPECTIVE DONOR

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8.0 HLA MISMATCHING AND DONOR/RECIPIENT CROSSMATCHING

An accredited histocompatibility laboratory is essential to support a living donor kidney transplant programme. Donor/recipient matching and crossmatching policies should be jointly established with the clinical transplant team and laboratory representation is essential in pre-transplant discussions concerning the selection of potential donors and in post-transplant case conferences. Close collaboration between transplant clinicians and the histocompatibility laboratory ensures the provision of clinically appropriate tests.

8.1 DONOR SELECTION

8.1.1 Requirements of the Human Organ Transplants (HOT) Act 1989

Current legislation under the Human Organ Transplants (Establishment of Relationship) Regulations 1998 incorporated into the Human Organ Transplants Act 1989 state that for living donor transplantation the genetic relationship between the proposed donor and recipient has to be established by means of genetic tests based on DNA variations. The tests need to be specified and the results interpreted by an 'Approved Tester' appointed by the Department of Health. He/she must be satisfied that the claimed genetic relationship is established. Testing of additional family members may be required to confirm the relationship.
Advice on this is provided by an Approved Tester. Approved Testers must fulfil their responsibilities under the Act including receipt of signed statements claiming a relationship, documented blood samples, completion of specified tests, recording and long-term storage of the test results, formal reporting and participation in the Royal College of Pathologists audit. Testers have to be aware of the limitations of the specified tests, report accordingly and understand the penalties defined in the Act.

For living unrelated transplants or in cases when a genetic relationship cannot be established, the case is currently referred to the Unrelated Live Transplant Regulatory Authority (ULTRA) via the ULTRA Secretariat at the Department of Health.

These arrangements will be subject to significant alteration when the HOT Act is repealed by the Human Tissue Act 2004, which comes into force in April 2006 (see section 2) and guidance will be updated accordingly.

8.2 HLA TYPING AND MATCHING

In the absence of preconditioning protocols, the choice of a living donor is restricted by the requirement for ABO blood group compatibility. HLA mismatching by DNA methods should be performed for potential donors and recipients (1).

Transplants between siblings offer the best opportunity for a well matched graft because of inheritance of HLA genes; siblings have a 1 in 4 chance of sharing both HLA bearing chromosomes (haplotypes) and of sharing no HLA haplotypes and a 1 in 2 chance of sharing one HLA haplotype. Parents and children share at least one HLA haplotype but may fortuitously share more HLA specificities.

Kidney transplantation from an offspring to the mother and from a father to the mother of his children has to be approached with care because of the possibility of pregnancy-related HLA-specific sensitisation. Where HLA sensitisation is excluded and a negative crossmatch is achieved, international data (Collaborative Transplant Study [CTS] and United Network for Organ Sharing [UNOS]) suggests that transplant outcomes are equivalent to that for other non-HLA identical living donor transplants (2, 3).

A widely cited publication of the experience of living unrelated spousal donor kidney transplantation in North America (3) established that graft survival rates for such transplants is equivalent to that of HLA mismatched living related donor kidney transplants. This equates with the current UK experience (See Table 11.1) CTS data on outcome of living donor kidney transplants found a significant reduction in graft survival when transplants were mismatched at HLA-A, -B and -DR (2).

8.0 HLA MISMATCHING AND DONOR/RECIPIENT CROSSMATCHING

Recent CTS analysis of more than 5000 living unrelated donor transplants performed between 1995 and 2002 shows a highly significant influence of HLA matching on graft survival (4), but graft survival remains superior to that of deceased donor transplantation.

A key point to remember is that when a poorly matched kidney transplant fails because of rejection the recipient is at high risk of becoming highly sensitised (5), restricting options for repeat transplantation. This is relevant for paediatric recipients who are likely to require re-transplantation within their lifetime and for whom avoiding sensitisation, particularly to common antigens, is important. It is not uncommon to list a child on the waiting list excluding parental antigens to avoid sensitisation against a prospective living donor in the future. In the context of older spouse couples, where a second transplant is unlikely, the benefits of living donor transplantation outweigh the risks of sensitisation.

Best Practice:
In the absence of a preconditioning programme, HLA typing of potential donors should not be performed until ABO blood group compatibility with the recipient is established. UK Guidelines for transplantation across ABO blood group barriers are currently being prepared by the BTS. (see section 12.1) When there is an option of selecting between living donors, then HLA matching should be considered a benefit, particularly in reducing the possibility of subsequent sensitisation. This is particularly important for younger recipients where repeat transplantation may be required.

Summary point:
Zero HLA-A, -B, -DR ("000") mismatched living related donor kidney transplants have the highest survival rates. If a well matched transplant fails, the recipient is less likely to become sensitised to non-self HLA.

8.3 RECIPIENT ANTIBODY SCREENING

The Histocompatibility laboratory must have comprehensive, accurate and sensitive screening programmes for the detection and definition of HLA class I (HLA-A, B, Cw) and Class II (HLA-DR, DQ) specific antibodies. Recipients should be screened for the presence of clinically relevant, potentially harmful HLA-specific antibodies in a manner equivalent to that for patients awaiting transplantation from a deceased donor. In order to define an individual's sensitisation status and interpret antibody screening results it is essential for the laboratory to have accurate information about the timing and nature of potential sensitising events. These include transfusions, pregnancies (including miscarriages), infections and previous transplants together with information on immunosupression with antibody therapy. This information will facilitate identification and definition of unacceptable HLA specificities and false positive antibody screening results.

Recipient serum samples must be taken at least every three months for antibody screening and at 14 days and 28 days following transfusion with any blood products.

A number of techniques are used in the laboratory for the definition of sensitisation including the complement dependent cytotoxicity assay, ELISA (enzyme linked immunosorbent assay) and flow cytometry based systems (6-11). As no single technique can provide complete information, it is recommended that a combination of methods is used to establish a patient's antibody profile. An accurate report of the patient's sensitisation status can only be made after careful interpretation of test results.

In normal situations post transplant serum samples should be obtained monthly for the first three months, quarterly up to one year and annually thereafter for antibody monitoring.

8.0 HLA MISMATCHING AND DONOR/RECIPIENT CROSSMATCHING

Summary point:
Screening of potential living donor kidney transplant recipients for clinically relevant antibodies is important for ensuring optimal donor selection and graft survival.

8.4 THE DONOR/RECIPIENT CROSSMATCH TEST

A donor-recipient crossmatch test is performed to determine whether there is pre-existing sensitisation to a specific donor. Kidney transplant units should define their own protocol for proceeding to transplant based, on immunological risk in combination with clinical practice (1).

A positive crossmatch test indicating donor-specific IgG antibodies present at the time of a proposed transplant therefore vetoes living donor kidney transplantation unless a preconditioning protocol is in place or the antibody responsible has been shown to be clinically irrelevant. In such circumstances there must also be the expertise, facilities and protocols to manage rejection caused by a rapid reappearance of increased levels of donor-specific antibodies. The BTS are currently preparing Guidelines to facilitate expansion of transplantation in this area in the UK. The crossmatch result must always be interpreted in the light of full antibody screening results, clinical events and sensitisation history. Performing an auto-crossmatch using the patient's own serum and cells to determine the presence of autoreactive antibodies can assist in the interpretation of a crossmatch result. The crossmatch test should be performed at an early stage in the assessment of a prospective donor so that if it is positive further unnecessary evaluation can be avoided.

The final crossmatch should be performed on serum sample collected within one to two weeks of the planned date for transplantation to confirm that it is safe to proceed. This time-frame minimises the risk of a sensitising event occurring between the last compatible crossmatch and the date of surgery but allows sufficient time to repeat testing prior to transplantation if there is a problem with the initial crossmatch. Blood transfusion after the final crossmatch, excluding peri-operative requirements, should be avoided whenever possible. If it is essential then transplantation should be deferred until at least two weeks later and following repeat crossmatching.

The technique used for the crossmatch test should be sensitive and clinically relevant. Crossmatch tests should be capable of distinguishing T lymphocyte and B lymphocyte populations and should discriminate between IgG and IgM (irrelevant autoreactive) antibodies. The use of a flow cytometric technique is recommended, particularly for sensitised patients and re-transplantation, as the conventional cytotoxic crossmatch is not sufficiently sensitive to detect all clinically relevant antibodies. If a sensitive antibody screening technique, such as ELISA, has been used and the recipient is consistently negative for HLA specific antibodies, then a flow cytometric crossmatch may not be essential.

It is important to select carefully the recipient serum samples to be used in the crossmatch test; knowledge of potential sensitising events, such as blood transfusions, will strongly influence the samples selected. Particular attention should be paid to consider samples that represent each of the antibody specificities defined in the patient's antibody profile and to the timing of samples with respect to the planned date for transplantation.

Careful consideration must be given to the sensitisation status and crossmatch results for proposed transplants where donor specific sensitisation through previous pregnancy may have occurred; offspring to mother or male to female partner donation. Donor specific blood transfusions may be performed in these instances in an attempt to reveal possible sensitisation by provoking an anamnestic antibody response. If this approach is used it should be performed in close collaboration with a consultant haematologist.

8.0 HLA MISMATCHING AND DONOR/RECIPIENT CROSSMATCHING

Comprehensive information about antibody screening and crossmatching can be found in the BSHI /BTS 'Guidelines for the Detection and Characterisation of Clinically Relevant Antibodies in Solid Organ Transplantation' (1).

Best Practice:
Kidney transplant units and Histocompatibility laboratories should agree a protocol defining crossmatch results that constitute a veto to transplantation. This should be evidence-based.

A pre-transplant serum sample collected within one week of the planned date for transplantation must be tested in a sensitive crossmatch and if the crossmatch test is positive transplantation should not usually be performed, unless the antibody is shown to be clinically irrelevant.

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9.0 DONOR FOLLOW-UP

9.1 ARRANGEMENTS FOR FOLLOW-UP

Early follow-up of the donor, within the first few weeks of surgery, is essential to ensure that he/she has made a satisfactory recovery from the operation. In the event of an unsuccessful transplant it is important to provide adequate emotional as well as physical support for the donor, including access to specialist psychological services (see section 4.4). Current practice with respect to long term follow-up varies widely between centres. In 1999, a survey of 28 UK centres reported their policy on long-term follow-up of living donors (1). 18 of the centres arranged life-long follow-up, 7 arranged limited follow-up (usually several years) and 3 centres did not follow-up the donors in the long-term (1). In the US, only 13 % of UNOS approved centres recommend indefinite donor follow-up (2).

A recent international consensus meeting on the care of the living donor emphasised that after donation the transplant centre has a responsibility to encourage and facilitate the long term follow-up of the donor, particularly for patients with pre-existing or acquired conditions that potentially place the donor at greater risk (3). These would include hypertension, obesity, diabetes and proteinuria. This follow-up in the UK could be provided by the transplant centre, the referring nephrology unit or the donor's General Practitioner. For overseas donors, returning to their country of origin, the principle of life-long follow-up should be encouraged but cannot be enforced or coherently monitored. In many countries, medical consultation/treatment is paid for by the individual and it is unrealistic for the transplant centre in the UK to do more then properly advise donors about the recommended follow-up.

The consensus report (4) also emphasises the need for a long-term comprehensive national registry of living donors in order to determine whether the incidence of medical risk factors and renal dysfunction is different from the general population. The UK is in a strong position to contribute to comprehensive follow-up data following donor nephrectomy. UK Transplant established the Living Donor Registry in 2000 and this collects pre-and post-operative data on all donors. All units in the UK should submit data on all donors to this registry.

For donors who travel from overseas to donate, there are implications for long-term follow-up arrangements and access to data once they return to their country of origin, particularly in countries where living donor transplantation is not an established practice or where individuals pay for healthcare. These donors should be provided with written advice about appropriate annual monitoring. However, it is difficult to ensure that robust arrangements are put in place and it is rarely possible to collect accurate data for the UK Living Donor Registry on overseas donors.

Best Practice:
Donors should be followed up to facilitate the collection of data on long term morbidity and mortality. Information should be submitted for inclusion in the UK Living Donor Registry. Life long follow-up is recommended and this should be offered locally or at the transplant centre according to the wishes of the donor.

9.2 THE UNSUITABLE DONOR

An area that is easily overlooked is the care and follow-up of patients who start the donor assessment process but who do not subsequently donate. If this is the result of concerns about the potential donor's health, it is essential that appropriate arrangements be made for any necessary further investigations and management. A donor who is unsuitable for other reasons (for example a positive cross-match) may need additional emotional support as they could cinsider that they to have "failed" the recipient - and blame themselves inappropriately for any subsequent adverse outcome for the recipient (see section 4.4).

9.0 DONOR FOLLOW-UP

9.3 PREGNANCY FOLLOWING KIDNEY DONATION

Many centres consider women of childbearing age as potential living donors. Pregnancy has a number of well-documented effects on the kidney raising the possibility that these may have an adverse effect in an individual with a solitary kidney. The information in this area is relatively limited. A study of 39 pregnancies in 23 women with 32 viable births revealed no significant problems and in particular no significant hypertension or proteinuria (5). Another study of 23 viable births in 14 kidney donors reported no significant problem (6). The presence of a solitary kidney does not appear to pose a significant risk during the course of a normal pregnancy. However, close follow-up is advisable in donors during pregnancy and periodic assessment of serum creatinine and creatinine clearance in addition to standard care, including urine culture and blood pressure should be undertaken.

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10.0 REIMBURSEMENT OF LIVING DONOR EXPENSES

10.1 CONTEXT

The reimbursement of legitimate expenses to a living donor, including loss of earnings, which are directly attributable to the organ donation, is supported by the Department of Health (DH) (1-2). Reimbursement does not contravene the current UK legislation, or that which will replace it in the near future, which forbids payment for supplying an human organ, provided that the donor does not gain any financial advantage as a result (3,4).

Whilst the NHS is not legally obliged to make such payments, it is recognised by the DH that the most cost effective treatment for end stage renal disease is renal transplantation and that the associated costs incurred as a direct result of performing a living donor transplant are justified. The DH encourages suitable arrangements to be made as part of local commissioning agreements between the recipient's Primary Care Trust (PCT) and the NHS Trust in which the transplant is performed. Such arrangements fall under the specialised commissioning groups and the method of making a claim should be made explicit to all relevant parties.

The Guidance makes recommendations about the nature and size of claims, taxable income and other sources of reimbursement that may be available to the donor (2) (see Appendix 10.1). There are separate arrangements in Scotland, which have been prepared by the Scottish Executive Health Department for NHS boards (5).

10.2 PRACTICAL CONSIDERATIONS

The system of local resolution between PCTs and NHS Trusts presents a challenge in terms of standardising practice for donor reimbursement. Nationally, there are excellent examples of effective systems in place but these arrangements have not been universally adopted and many transplant centres experience difficulties in resolving claims in a timely manner when most benefit is afforded to the donor and their family. The model in Figure 10.1 is recommended as best practice

10.3 DONORS FROM OVERSEAS

The Guidance emphasises the importance of avoiding donor reimbursement from the recipient or his/her family, which could be seen as an inducement to donate and, therefore, illegal. This can be problematic when donors require visas to travel from overseas into the UK. The immigration authorities require evidence that a person entering the UK is financially self-sufficient or funded by their family; which conflicts with the position on reimbursement and can result in delay in issuing visas to overseas donors. In addition, the donor is unique in that he/she is entitled to travel to the UK to receive NHS treatment (for the purposes of donor assessment and surgery). A letter from the transplanting centre in support of the donor's visa application, to be submitted with the application and copied to the potential donor, is recommended as a minimum standard and should include the following points:

- The purpose of the application
- The type and duration of the visa required (a minimum of 6 months is usually necessary)
- Relationship between donor and recipient
- The reason for the choice of donor i.e. no suitable donors living in the UK
- Any preliminary medical information to support the potential suitability of the donor (Blood grouping and previous medical history are suggested as a minimum)
- The treatment plan for the donor and estimated length of stay in the UK. It should be explicit that the donor has been informed that there is 'no right to stay' in the UK beyond that which is clinically necessary and that there is an expectation that he/she will return to the country of origin after a suitable period of convalescence post donation*

** Based upon experience at University Hospital Birmingham NHS Trust*

10.0 REIMBURSEMENT OF LIVING DONOR EXPENSES

- The DH position on entitlement to NHS treatment/donor reimbursement.
- The relative cost-effectiveness of living donor transplantation versus dialysis on the UK health economy.
- Contact details for further information from the transplanting centre

Applications are frequently refused on the first submission and direct contact between the transplant centre and relevant embassy/high commission is recommended in such cases to achieve the desired outcome.

There are a number of logistical issues to consider in the context of overseas donors. Currently, centres largely make individual arrangements according to what works or is realistically achievable, highlighting the need for further work to establish coherent processes and improved guidance in this area. This section of the Guidelines will be updated as new developments progress.

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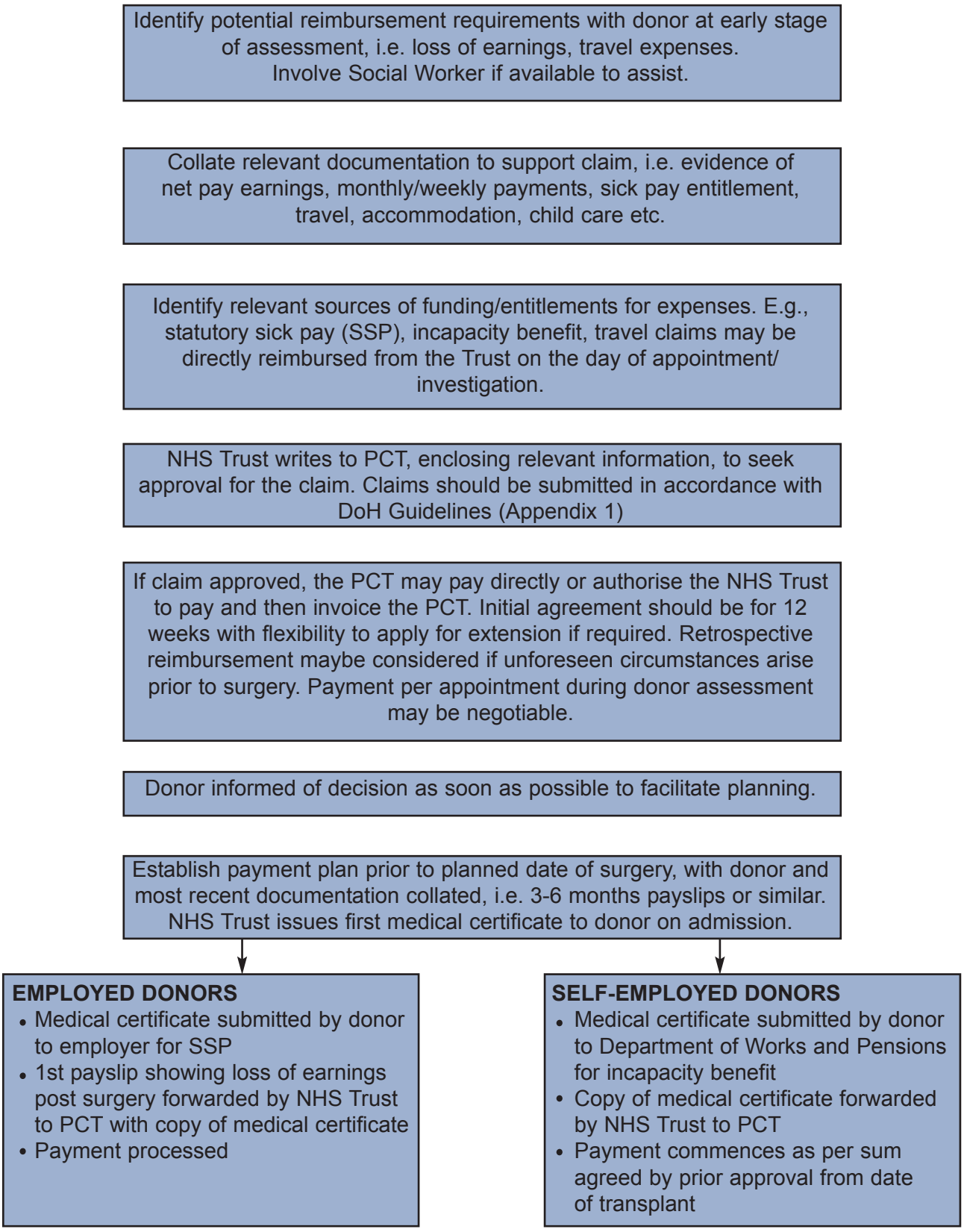
10.0 REIMBURSEMENT OF LIVING DONOR EXPENSES

Figure 10.1 Best Practice Model for Reimbursement of Living Donor Expenses
(reproduced courtesy of Royal Liverpool University NHS Trust)



10.0 REIMBURSEMENT OF LIVING DONOR EXPENSES

Appendix 10.1

Reimbursement of living donor expenses by the NHS

The Department of Health with the help of the Inland Revenue has prepared the following explanation of the proper reimbursement of a living organ donor's expenses.

Background

The Human Organ Transplants (HOT) Act, 1989 forbids the offer or payment of any inducement for the supply of a human organ. However, it does not prohibit the payment of reasonable expenses to a donor for travel and accommodation and any loss of earnings incurred if directly attributable to his/her donation of an organ.

NHS trusts and PCTs are permitted to make such payments and should do so if the live transplant is permitted under the HOT Act. The NHS is not legally obliged to make such payments. However, as a renal transplant is the most cost-effective treatment for end stage renal failure, and a live donor transplant may be the only option for a patient in liver failure, payment of the cost of the donor operation, and any associated donor expenses, is justified.

Renal transplantation now comes under the specialised commissioning groups' arrangements. Whether the NHS Trust or a PCT actually refunds the donor is a matter for those commissioning arrangements but should be agreed beforehand and the method of making a claim and receiving payment explained to all concerned. The service agreement should be explicit about how any such payments are to be made, whether by the Trust or by an application to a PCT.

Any payments to living donors should ensure that, within reason, the donor is no worse off as a result of the donation, but neither should they gain any financial advantage. Any payments in excess of the amount needed to reimburse losses would constitute a payment for the donation and breach the HOT Act, 1989.

Reimbursement

The level of any reimbursement will depend on any other sources of reimbursement available to the donor. Absence from work could be 6-12 weeks and those in employment may not be entitled to be paid their full salary (or even a reduced/basic rate) for all periods of sickness absence. An employer may not be willing to pay anything for "voluntary sickness" (although many employers will wish to fully support such a generous act). Some may be able to claim statutory sick pay but will probably wish to contact their local social security office as well as discussing it with their employer. If the donor is a member of a union they may want to seek advice on their rights from their union.

It may be more difficult to calculate expenses and travel costs if the donor is coming from abroad. It is of particular importance that any such expenses are only reimbursed by a PCT or Trust and not by the family of the recipient. Any payment, even of reasonable expenses, by the family could be interpreted as an inducement to donate.

The final decision as to whether expenses will be paid rests with the service commissioners following consultation with the Trust.

Personal expenses

Reimbursement of personal expenses such as transport costs should be repaid in full on provision of receipts or in the case of e.g. mileage at an agreed rate such as the standard NHS rate. Such payments are legal under the HOT Act and are not subject to any tax liability.

Loss of earnings

Payments for loss of earnings are legal under the HOT Act but the method of payment and position with respect to any tax liability depends on the employment status of the individual.

- Employed persons - earnings arising from their employment are normally subject to tax and National Insurance contributions and paid through PAYE. Reimbursement should be paid of net income and will not be taxable.

10.0 REIMBURSEMENT OF LIVING DONOR EXPENSES

Some employers may continue to pay basis pay but the donor may lose supplementary pay in the form of commission or tips. Such losses may be made up on suitable proof of average overall earnings. Exceptionally, if the person is on unpaid leave for several weeks, they may need to make voluntary payments to make up lost pension contributions to e.g. a stakeholder pension or Class 3 additional voluntary National Insurance contributions for a state pension. Such voluntary contributions can be reimbursed without any tax liability. In view of the short time they are away from work live donors should not need to make additional National Insurance contributions but if they are unsure they should contact their tax office.

- Self-employed persons - will be liable for tax on any money they receive which is not specifically excluded. Reimbursement of loss of earnings should be paid on gross income. This will enable the donor to pay tax, National Insurance and pension contributions for the period they were unable to work. Proof of gross income will be required such as a copy of the income and expenses page of their tax return. Although liable for tax, such payments are legal under the HOT Act as long as there is no overpayment. In the case of very high earners, full reimbursement of lost earnings may not make the transplant cost-effective. Trusts may wish to offer reim bursement up to the average national wage. There is no bar to reimbursements in excess of the average in exceptional circumstances as long as it is in the best interests of the recipient.
- Non-employed persons - are not liable for tax and would normally only be reimbursed personal expenses. However, they might lose benefit if not available for work for several weeks. Such benefit losses should be reimbursed
- Retired persons - are not liable for tax but now only lose state pension if for any reason they are in hospital for more than 52 weeks.

Child Tax Credit and Working Tax Credit

A person's entitlement to Child Tax Credit will not be affected by the fact that (s)he is a live donor. A short absence from work should not affect a donor's entitlement to Working Tax Credit, including the child care element, because assuming the donor plans to return to work as soon as (s)he has recovered, the Revenue would not regard the absence as affecting the donor's "usual working hours". When entitlement to either or both of the tax credits is assessed, only taxable income is taken into account. So if donors receive non-taxable income, they are not required to report it to the Inland Revenue. Donors who need further information should contact the Tax Credit Helpline on 0845 300 3900 for further advice.

Contact

Transplant Policy Team, Department of Health, Enquiries: 020 7972 4921

Renal information

11.0 RECIPIENT OUTCOME AFTER LIVING DONOR KIDNEY TRANSPLANTATION

11.1 CLINICAL AUDIT

Clinical audit is integral to practice within the transplant unit. Recipient survival, morbidity and graft survival depend critically upon a number of case mix factors such as age and co-morbidity of the transplant population. These in turn depend upon the criteria for selecting patients as suitable recipients and, more remotely, on the criteria for acceptance on to dialysis.

11.2 PRIMARY NON-FUNCTION

95% of living donor kidney transplants function immediately. Absence of urinary output from the transplanted kidney in the immediate post transplant period is a cause for concern and requires emergency scanning to confirm graft perfusion.

11.3 MEASURING OUTCOME AFTER LIVING DONOR TRANSPLANTATION

Outcome after living donor transplantation can be measured by recipient and graft survival. Secondary measures of outcome are the incidence of acute graft rejection, chronic transplant nephropathy and tumours. All UK transplant units supply data to UK Transplant (UKT) on recipient and graft survival and this enables centre specific and comparable data on outcome to be compiled.

11.4 RESULTS FROM THE OPTN/UNOS REGISTRY

A recent report of the OPTN/UNOS registry in the United States analysed graft survival in 57,612 recipients of primary renal allografts performed between 1998 and 2002 (1). In this analysis patient death was counted as graft failure. 23,404 of the grafts analysed were from living donors. Graft survival was best for HLA identical sibling donors, with a five-year graft survival of 87%. For genetically unrelated transplants (spousal and others), five-year graft survival was indistinguishable from that for one-haplotype-matched sibling transplants at 78-81%. In terms of HLA matching, living donor transplants with no HLA mismatch (MM) grade had the best five year graft survival (87%), but thereafter HLA MM grade did not influence 5 year graft survival which was similar for grafts with a 1-3 HLA MM grade and those with a 4-6 HLA MM (80% and 79%). The results for all types of living donor transplant were superior to those for deceased donor transplantation, where five-year graft survival was 66%.

11.5 RESULTS FROM THE UK TRANSPLANT DATA BASE

The following outcome data is derived from an analysis by UK transplant of 2322 living donor transplants performed in the UK from 1993 to 2002. The results are similar to those obtained from the OPTN/UNOS database. Overall patient survival is 98% at one year and 95% at five years Table 11.1.

Overall graft survival after living donor kidney transplantation was 93% at one year and 82% at five years. The relationship between donor and recipient and graft survival at one and five years is shown in Table 11.2. Recipients of a kidney from a genetically unrelated donor had excellent one year graft survival rates (93%) that were comparable to those seen in recipients of grafts from a genetically related donor. There were insufficient unrelated donor grafts with five-year follow-up data to enable analysis of five-year survival.

Analysis of the data according to HLA mismatch grade is shown in Table 11.3. The HLA mismatch grade had no effect on graft survival at one year. Five-year graft survival was, however, significantly lower in grafts with 2 and 3 HLA MM (83% and 79%) than those with zero or one HLA MM (both 85%), (Log-rank test, p=0.02).

The relationship between donor and recipient, according to degree of HLA MM and graft survival is shown in Table 11.4. As for the OPTN/UNOS data, HLA identical sibling transplants had a superior outcome although

11.0 RECIPIENT OUTCOME AFTER LIVING DONOR KIDNEY TRANSPLANTATION

HLA MM grade had only a small effect on graft survival for non-HLA identical sibling transplants and for parent to child transplants.

Standard:
Graft survival after living donor kidney transplantation should be at least 95% at one year and 85% at five years.

Standard:
Patient survival after living donor kidney transplantation should be at least 95% at one year and 90% at five years.

References

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Recipient outcome after living donor kidney transplantation - Transplant survival estimates

Table 11.1 Patient survival in living donor kidney transplants performed in the UK, 1993 - 2002

	Number of transplants[1]	Percent patient survival:			
		One year	(95% CI)	Five years	(95% CI)
Overall	**2040**	**98**	**(98 - 99)**	**95**	**(93 - 96)**

[1]Patient survival time is calculated from the date of first transplant, therefore retransplants are not included.

Table 11.2 Relationship between donor and recipient and transplant survival in living donor kidney transplants performed in the UK, 1993 - 2002

Relationship of living kidney donor to recipient	Percent of 2322[1] living donor kidney transplants in the UK	Percent transplant survival[2]			
		One year	(95% CI)	Five years	(95% CI)
Parent	44	92	(91 - 94)	81	(78 - 84)
Sibling	36	94	(92 - 96)	84	(81 - 87)
Other relative	5	96	(93 - 100)	82	(73 - 92)
Unrelated (80% of which were spouse/partner)	14	93	(91 - 96)		
Overall[2]		**93**	**(92 - 94)**	**82**	**(80 - 84)**

[1]Transplants with missing transplant survival times are not included.
[2]There are insufficient data to obtain five-year transplant survival estimates for unrelated transplants. Unrelated transplants are not included in the overall five-year transplant survival estimate.

11.0 RECIPIENT OUTCOME AFTER LIVING DONOR KIDNEY TRANSPLANTATION

Table 11.3 HLA mismatch and transplant survival after living donor kidney transplantation in the UK, 1993 - 2002

HLA-A, -B, -DR mismatches	Number of transplants[1]	Percent transplant survival[2]			
		One year	(95% CI)	Five years	(95% CI)
Zero	419	94	(91 - 96)	85	(80 - 89)
One	230	94	(91 - 97)	85	(80 - 91)
Two	606	93	(92 - 95)	83	(79 - 86)
Three	744	93	(91 - 95)	79	(76 - 83)
Four	136	93	(89 - 98)		
Five	128	94	(91 - 98)		
Six	53	87	(77 - 96)		

[1]Transplants with missing transplant survival times and transplants with missing HLA-A, -B and/or -DR mismatch information are not included

[2]Transplants with four, five or six HLA mismatches are mostly unrelated transplants. There are insufficient data to obtain five-year transplant survival estimates for unrelated transplants. Five-year transplant survival: zero and one HLA mismatches=85%, two and three HLA mismatches=81%, Log-Rank p=0.02.

Table 11.4 Relationship between donor and recipient, degree of HLA mismatch and transplant survival after living donor kidney transplantation in the UK, 1993 - 2002

Relationship of living kidney donor to recipient	Degree of HLA mismatch	Number of transplants[1]	Percent transplant survival:			
			One year	(95% CI)	Five years	(95% CI)
Sibling	000	337	94	(92 - 97)	85	(81 - 90)
	Non-favourable	421	93	(91 - 96)	81	(77 - 86)
Parent	000	74	90	(84 - 97)	81	(70 - 92)
	Favourable	228	92	(88 - 95)	83	(77 - 89)
	Non-favourable	727	93	(91 - 95)	80	(76 - 83)

[1]Transplants with missing transplant survival times, transplants with missing matchgrade information and transplants where the donor was not a sibling or a parent are not included.

12.0 THE HIGH RISK RECIPIENT

Living donor transplantation for high-risk recipients, i.e. potential transplant recipients who are at high risk of death or graft failure, requires special consideration. Such patients include those with severe cardiovascular disease, pulmonary disease, diabetes mellitus and obesity. It is important that both donor and recipient are given a realistic estimate of successful outcome prior to proceeding to transplantation. A key issue is that, whilst these patients may expect a relatively poorer outcome following transplantation when compared with individuals who are deemed to be at lower risk, the same would apply if they were on dialysis. Analysis of patients on dialysis has shown that survival is dependent on the cause of renal failure (1). For example, patients with diabetes mellitus may have a poor survival either on dialysis or with a transplant compared with individuals of the same age without diabetes. Other co-morbidities may play a role but the data for diabetes is the most complete (Tables 12.1 & 12.2). Factors that predict outcome in deceased donor transplantation are long cold ischaemia time (2) and delayed graft function (3). These are avoided with living donor transplantation and thus the proportional improvement in outcome for high risk recipients may be similar to that of low risk recipients. Whilst long term survival will not be comparable, living donor transplantation may be the best option for high risk patients provided that there is clear understanding of risk.

Summary Point:
Living donor transplantation may be the only option for individuals who have a poor outcome on dialysis treatment. High-risk recipients who are not suitable for deceased donor transplantation may still be eligible for a living donor kidney. Donor and recipient should be given a realistic estimate of the chance of a successful transplant outcome.

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12.0 THE HIGH RISK RECIPIENT

Table 12.1 Renal Registry Data

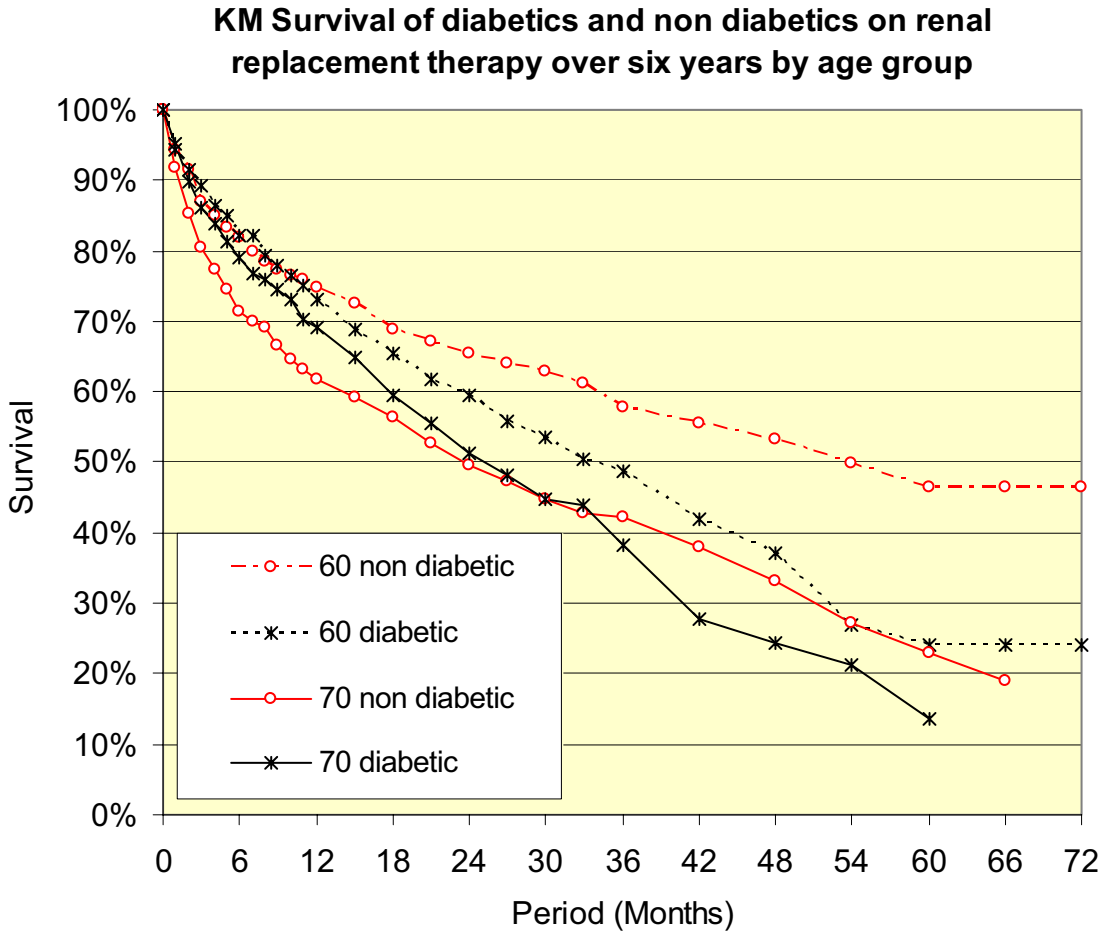
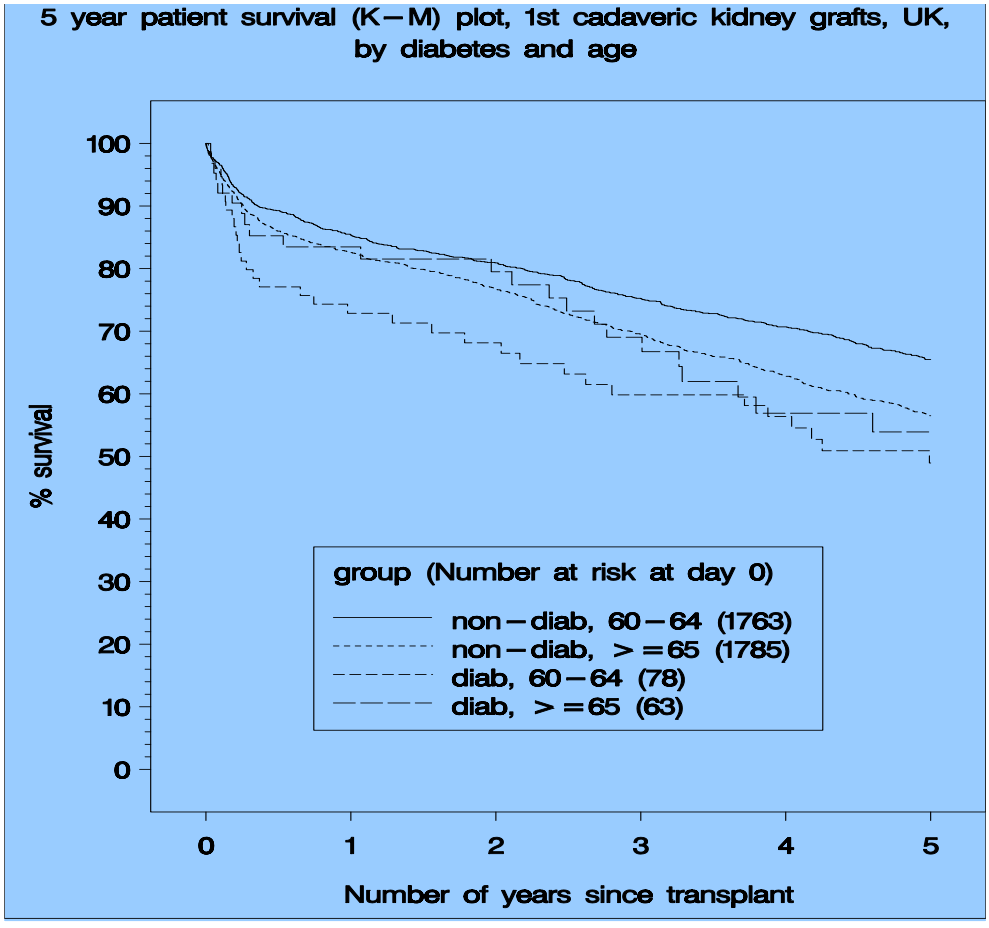


Table 12.2 UK Transplant Data



12.1 THE HIGH RISK RECIPIENT: THE HIGHLY SENSITISED RECIPIENT: DESENSITISATION AND ABO BLOOD GROUP INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION

This section to be augmented when the desensitisation working party reports

12.1.1 ABO Incompatible Transplantation from Living Donors

ABO incompatibility does not preclude renal transplantation. Approximately 20% of blood group A individuals (A2) express smaller amounts of A antigen than the majority (A1).

Blood group A2 kidneys may be successfully transplanted into some blood group O or B recipients who have low titres of anti A IgM antibody using standard protocols from cadaveric and living donors. (1)

Transplantation between A1 donors and the majority of recipients with normal or high anti A titres is still possible but requires a combination of immunological therapies which includes antibody removal, mono or polyclonal antibody treatment and splenectomy as well as conventional immunosuppression. (2,3)

Living donor transplantation facilitates pre transplant antibody removal which may take up to 24 hours to achieve.

Recent protocols have sought to avoid splenectomy and use pre-transplant immunoadsorption, anti CD 20 monoclonal antibody therapy +/- IV IgG as well as triple immunosuppression with CNI, MMF and steroids. (Reference 4)

Results appear to be comparable to ABO compatible living donor transplants although few long term data are available.

Several UK centres have started an ABO incompatible transplant programme and predict an increase in living donation of 10 to 20% as a consequence.

Summary Point:
ABO incompatible living donor transplantation is possible in specialised centres and may become generally available.

References

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3. Gloor JM et al. Transplantation 2003 75(7); 971-77 ABO-Incompatible Kidney Transplantation using both A2 and non-A2 living donors.
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13.0 RECURRENT RENAL DISEASE

A number of the diseases responsible for chronic renal failure may affect a renal allograft (1, 2). In some of these, the recurrence may have no impact on function during the lifetime of the transplant. Caution should be taken when interpreting the literature because of ascertainment bias. The important issues to consider are:

- The likelihood that a particular disease will affect a transplant. Prediction of recurrence rates is very difficult.
- Whether recurrence of disease will cause graft failure and if so how quickly
- Whether the risk of recurrent disease is more likely in a graft from a living
- Related donor
- Studies reported are often retrospective and from single centres.
- Recurrent disease is not reliably distinguished from de novo disease.
- Prospective protocol biopsies are not routinely used to evaluate the true recurrence rate.
- The impact of recurrence on graft survival and graft function should be interpreted in the context of the indication for the biopsy. Biopsies are often taken for proteinuria and declining renal function.

In deciding whether to proceed with living donor transplantation the donor and recipient should be advised that recurrence rate is difficult to predict. If there is recurrence, especially if it is associated with significant proteinuria and impaired renal function, then graft survival may be reduced. However, the risk of recurrence in itself does not preclude living donation.

References

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13.1 PRIMARY HYPEROXALURIA

Living donor kidney transplantation in this rare condition is controversial and specialist advice should be sought. Recent experience has led to a recommendation that combined liver and renal transplantation from a deceased donor is undertaken or that pre-emptive liver transplantation be performed (3-5). Some North American groups advocate early living donor kidney transplantation (3,6). Immediate graft function is essential to avoid rapid graft destruction from oxalate deposition. It is crucial to maintain a high urine output in the longer term to maintain adequate oxalate clearance, as the underlying metabolic defect persists after kidney transplantation alone.

References

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13.2 IgA NEPHROPATHY

IgA nephropathy commonly recurs following renal transplantation. The recurrence rate in one series, based on graft biopsy, has been reported to be around 80% in living related transplantation (7) and 60% in a series of deceased donor grafts (8). In most series histological recurrence rates have been reported at 26-46% (9-13). The clinical expression of the disease is variable and time dependent. Excellent short-term graft survival has been reported in those patients with early recurrence.

Graft loss during the first three years is uncommon. However, experience in recipients of deceased donor grafts, shows that long term graft survival in patients with IgA nephropathy may be compromised in those patients in whom recurrence is detected. Living donor transplantation is associated with increased recurrence and graft loss in some series but not in others. However, it is not contraindicated since recurrence is difficult to predict and the increased risk and impact on graft survival are small.

13.0 RECURRENT RENAL DISEASE

The recurrence rate in Henoch Schönlein Purpura is less well characterised. The patterns for recurrence appear to be similar to those reported for IgA nephropathy (14).

References

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13.3 MEMBRANOUS GLOMERULONEPHRITIS

The reported experience of recurrent membranous glomerulonephritis is small. There have been reports of recurrence within the first few months following living related transplantation (15-17). The largest series reported a recurrence rate of 29% in 30 patients at 3 years post transplantation and a graft survival of 52% at 5 years and 38% at 10 years (18,19). Living donor transplantation is not contraindicated for recipients whose original disease is membranous glomerulonephritis but both donor and recipient should be advised about the the possibility of recurrence which may lead to graft loss or reduction in graft survival.

References

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13.4 DIABETES MELLITUS

Biopsies of kidney allografts taken more than two years after transplantation in diabetic recipients show glomerular changes consistent with diabetic nephropathy (20). However, the latency between onset of the diabetic milieu and ESRF is sufficiently long that there is little clinical concern, at least in the medium term. A study of 265 diabetic renal allograft recipients found that none of the grafts were lost due to recurrent disease in the first ten years after transplantation (21).

References

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13.0 RECURRENT RENAL DISEASE

13.5 CYSTINOSIS

In this condition, deposition of cystine in the renal allograft is inevitable but there is no evidence that this has an adverse effect on graft survival. Living donor kidney transplantation in children with cystinosis offers them an opportunity for early transplantation and can therefore help to avoid stunting of growth.

13.6 AMYLOIDOSIS

Renal recurrence of amyloid is likely unless, in the case of secondary amyloid, the causal disease is rendered inactive. Amyloid deposition is relatively indolent although it was reported in 25% of biopsies from grafts in recipients with amyloidosis examined more than one year after renal transplantation (22). It is unlikely to cause renal dysfunction or nephrotic syndrome within 10 years of transplantation. Amyloidosis in the recipient is not an absolute contraindication to living donor transplantation but the effects of amyloid in other organs, particularly the cardiovascular system, should be thoroughly assessed before listing for transplantation.

Reference

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13.7 FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Recurrence of focal segmental glomerulonephritis (FSGS) is a significant problem after renal transplantation. The recurrence rate varies from 15% to 100% in different series (23-25). The wide distribution of rate of recurrence is in part because FSGS represents the histological description of renal injury. The histology of FSGS as seen in a 'remnant kidney' where the individual had severe hypertension, chronic pyelonephritis or reno-vascular disease carries no risk post-transplant. Nephrotic syndrome due to FSGS is a completely different matter.

Patients who are at highest risk of early recurrence leading to the development of significant proteinuria and graft dysfunction are individuals in whom the original disease had a fulminant course leading to ESRF within three years, those who had a recurrence in a previous graft and those who presented with FSGS before the age of 15 (26-29).

Living donor kidney transplantation in children with fulminant FSGS, therefore, carries a high risk of recurrent disease and premature graft failure. A histological diagnosis of FSGS should not preclude transplantation. Living donor transplantation should be avoided in patients with high risk of recurrence or be performed in high-risk cases after in depth discussion of the risks involved with all participants.

Best Practice:
Living donor kidney transplantation should only be performed in high-risk cases when the donor has a clear understanding of high graft loss in the recipient.
Re-transplantation from a living donor is reasonable if a previous graft showed prolonged function or was free of FSGS.

References

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13.0 RECURRENT RENAL DISEASE

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13.8 ALPORT'S, CRESCENTIC GLOMERULONEPHRITIS, VASCULITIS

Recurrent anti-glomerular basement membrane (GBM) disease in allografts is rare (30). One group has reported a histological recurrence of 50% in patients who receive a kidney transplant while circulating anti GBM antibodies are present but this is reduced to only 5-15% in patients who receive a transplant 6 months of more after the disappearance of anti GBM antibodies (31,32). Transplantation is usually delayed until at least 6 months after antibodies disappear (33). *De novo* anti-GBM disease has been reported occasionally in patients with Alport's syndrome, due to the recognition of "normal" donor GBM epitopes as "foreign" by the Alport's recipient. This is not sufficiently common to constitute a contradiction to transplantation in Alport's patients.

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis recurs in approximately 20% of recipients, in comparison to a 30-45% relapse rate in untransplanted patients. Relapses have been reported to occur from 4-89 months after kidney transplantation. Renal and extra-renal manifestations occur but graft loss only happens in the minority (30). Patient and graft survival post transplantation appears to be equivalent in ANCA associated vasculitis groups as compared with the general transplant population. ANCA titres do not correlate with disease recurrence. It would be prudent to ensure patients with ANCA-associated vasculitis are in clinical remission before considering transplantation although the optimal duration of remission is unclear.

References

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13.9 HAEMOLYTIC URAEMIC SYNDROME

Haemolytic uraemic syndrome (HUS) can be divided into Shiga-toxin associated HUS (most commonly with diarrhoea and coincident with verocytotoxin producing coliforms), idiopathic HUS and inherited HUS (34). HUS may also be secondary to drugs and occurs rarely in other situations such as pregnancy or complicating connective tissue diseases, transplantation or glomerulonephritis. A recent meta-analysis considered ten studies, and included 159 recipients who received a renal transplant because of HUS (35). The overall recurrence rate of HUS was 28% and one-year graft survival when recurrence occurred was only 33%. Recurrence is uncommon after Shiga-toxin associated HUS (36). Inherited HUS, although rare, frequently recurs after transplantation and it is important, therefore, to explore the family history in HUS (37, 38). In idiopathic HUS there is also a high chance of recurrence after transplantation (2 out of 5 cases) (39, 40,). The reported two-year graft survival in this setting is very poor at 35%. (41). Recurrence was associated with an older age of onset, rapid progression of the original disease, earlier transplantation, living related transplantation and the use of calcineurin inhibitors (35). Recent advances in the understanding of the molecular pathogenesis of inherited HUS and TTP may help identify more clearly those patients at increased risk of recurrence (42, 43).

13.0 RECURRENT RENAL DISEASE

Best Practice:
Living donor kidney transplantation should be avoided in recipients with inherited or idiopathic HUS because of the likelihood of graft loss from recurrence. Shiga-toxin associated HUS does not commonly recur and is not a contraindication to living donor transplantation.

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13.10 SYSTEMIC LUPUS ERYTHEMATOSUS

Recurrent lupus nephritis is reported to occur in around 2-4% of patients requiring kidney transplantation because of ESRD due to Systemic Lupus Erythematosus (SLE) (44-48). Recurrence of nephritis does not always lead to graft failure. Recent data provides conflicting evidence as to whether SLE results in inferior patient and graft survival (44-48). However, in the majority of patients the rate of recurrence is low and disease activity is reduced. Therefore, transplantation is not contraindicated in patients with SLE. In series reporting increased graft loss in patients with SLE, early graft loss due to thrombotic events may be a factor. Recently, it has been shown that thrombotic events are associated with antiphospholipid antibodies and these are found, with increased frequency in SLE (49, 50). In patients with SLE who have raised antiphospholipid antibodies, careful attention should be paid to peri-operative anti-thrombotic prophylaxis. The control of SLE activity should be optimised before renal transplantation is undertaken although there is no good evidence that this prevents recurrent nephritis.

Pre-transplant serological indicators of SLE activity, duration of dialysis and histological classification of lupus nephritis are not reliable predictors of recurrent disease (44,45,47). The presence of autoreactive antibodies in patients with SLE may make the interpretation of a crossmatch result between donor and recipient difficult. An auto-crossmatch is recommended in order to assist with the interpretation of such results (see section 8.4).

Best Practice:
Living donor kidney transplantation is not contraindicated in SLE but optimal control of disease activity should be achieved before transplantation is undertaken.

References
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13.0 RECURRENT RENAL DISEASE

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13.11 MESANGIOCAPILLARY GLOMERULONEPHRITIS

Type I mesangiocapillary glomerulonephritis (MCGN) recurs in around 30% of renal allografts and recurrence leads to graft loss within four years in about a third of such cases (51). The risk of recurrence approaches 80% in subsequent grafts (52). Both donor and recipient should be warned of the risk of graft loss from recurrent MCGN before transplantation is undertaken. Type II MCGN is the primary glomerulonephritis that is most likely to recur after renal transplantation and does so in over 90% of cases. The histological changes can be seen as early as one week after transplantation (53) and clinical signs are usually evident within one year. However, the long term outcome after transplantation is variable. About 10% of grafts fail within five years (53) but many patients have urinary abnormalities with stable renal allograft function for years. Many clinicians regard either an indolent native course of glomerulonephritis or the long survival of a primary graft as suggesting a good prognosis for subsequent grafts.

Best Practice:
Living donor kidney transplantation should only be performed in high-risk cases when the donor has a clear understanding of high graft loss in the recipient. Re-transplantation from a living donor is reasonable if a previous graft showed prolonged function. In MCGN type I, the donor and recipient should be informed of the risks of recurrence as with other forms of recurrent disease.

References

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Summary Point:
There is a wide range of diseases that cause kidney failure and may recur in the renal allograft. Both the recurrence rate of such diseases and the impact on graft function and survival is hard to predict but this should not preclude consideration of living donor kidney transplantation. Careful evaluation of the potential risks involved including the aetiology of the original disease, the likelihood and speed of recurrence and whether or not there is an increased risk associated with a living donor kidney must be considered. In some cases, such as fulminant FSGS, MCGN and inherited or idiopathic HUS, the risks may be considered inappropriately high to proceed to transplantation.The recipient and donor must be fully appraised of the risks, where known, of recurrence, premature graft failure and potential co-morbidity. Where there are identifiable risks associated with current disease activity in the potential recipient, such as vasculitis or SLE, optimum control of the underlying disease is essential before proceeding to transplantation.

14.0 LIVING DONOR KIDNEY TRANSPLANTATION IN CHILDREN

When transplanting children from living donors, there are some specific issues that require consideration. The purpose of this section is to highlight some of the key areas that warrant special mention, primarily in the context of the transplant operation and peri-operative management. As paediatric recipients are likely to require re-transplantation during their lifetime, every effort should be made to minimise HLA mismatches to reduce the risk of future sensitisation (see section 8.2).

In general, children who are more than 10kgs in weight are suitable to receive a kidney from an adult living donor. The kidney is usually placed in the right side of the abdomen. The intra-peritoneal approach allows access to the mid-aorta and vena cava for attachment of the renal vessels. Some surgeons prefer the extra-peritoneal approach to the great vessels. This decision is usually dictated by the size of the recipient but there are other factors that may influence this, including the presence of a thrombosed inferior vena cava (IVC) or other anatomical abnormalities.

Standard abdominal closure following transplantation onto the iliac vessels in small children (or onto the aorta and IVC in those closer to the minimum weight) may compromise graft perfusion. Porcine dermal collagen grafts inserted as a patch closure of the abdominal muscle reduce the graft compression and do not lead to herniation (1).

The implantation of an adult kidney into a paediatric recipient requires close cooperation between the surgical and anaesthetic teams. Meticulous attention needs to be paid to the child's intravascular volume status. When the aortic and inferior vena cava clamps are released, the transplanted organ and lower extremities fill with blood, potentially resulting in severe hypovolaemia unless adequate volume loading has taken place. Washout of the organ preservation fluid into the child's circulation may reduce core temperature and produce severe hyperkalaemia. Careful monitoring and replacement of on-going fluid loss is required, remembering that the urine output from the adult kidney may be significant. In the early post-operative phase, particular attention should be paid to fluid and electrolyte balance because of the large volumes of urine that can be passed. Urine output and insensible losses are replaced initially with 2.5% glucose/0.45% saline, volume for volume on an hourly basis. Plasma electrolytes are checked at 2-4 hourly intervals for the first 12 to 24 hours and replacement fluids should be adjusted according to these results. Central venous pressure (CVP) monitoring is mandatory and the CVP should be maintained at 5-10cmH2O in the spontaneously breathing patient, with intravenous normal saline or by the administration of an alternative colloid to correct hypovolaemia.

Where intra-peritoneal surgery has taken place, a post-operative ileus may develop and the child may not be able to commence feeds for a number of days. In such situations careful consideration should be given to administering immunosuppressive agents via the intravenous route where it is possible and safe to do so. The risk of vascular thrombosis is greater in this group than in larger/adult recipients and the use of anti-platelet therapy may be advocated.

It may be necessary to carry out the donor and recipient procedures in separate hospitals and, provided that the kidney is transported safely and efficiently between the two centres to minimise cold ischaemic time, there is no impact on the incidence of primary graft function (see section 6.5.1). Consideration should be given to the geographical separation of the donor and recipient during the post-operative period and the emotional impact that this may have on the donor, recipient and carers. Provision should be made e.g. via Webcam technology or similar, to facilitate contact between the donor, child and their carers at this time.

Reference

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