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UNITED KINGDOM

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# GUIDELINES

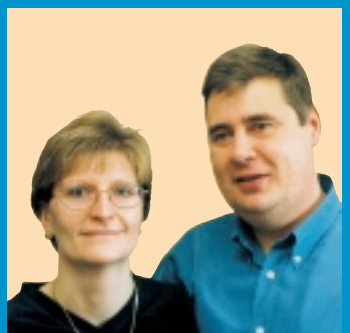
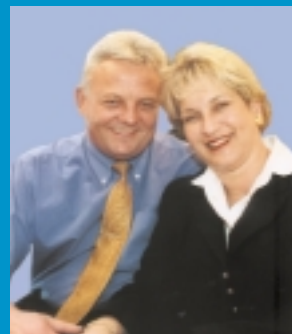
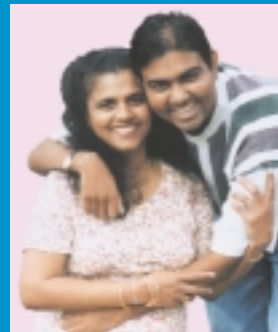
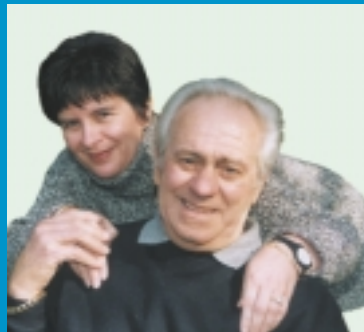
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FOR LIVING DONOR KIDNEY

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TRANSPLANTATION

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UNITED KINGDOM

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**GUIDELINES**

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TRANSPLANTATION

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These guidelines were prepared by a working party of the British Transplantation Society and the Renal Association. Their aim is to assist clinicians and other healthcare workers involved with living donor kidney transplantation.

Further copies of this document are available from Triangle.



The Renal  
Association

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January 2000

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## 1.1 THE NEED FOR GUIDELINES

The setting of standards and the provision of clinical guidelines describing best practice are important in all areas of clinical medicine. The Renal Association published clinical guidelines for the practice of renal medicine in 1996 and included in this document were the first published UK guidelines for renal transplantation.<sup>(1)</sup> The British Transplantation Society (BTS), recognising the need to set standards in clinical transplantation, published, in 1998, “Towards standards for organ and tissue transplantation in the United Kingdom.” This document set out standards of care in all aspects of organ and tissue transplantation.<sup>(2)</sup> It makes a number of important recommendations concerning living donor kidney transplantation, although coverage of this important area in the original document was, through necessity, relatively limited.

Living donor kidney transplantation provides patients in end-stage renal disease (ESRD) with the best chance of good long term rehabilitation. There is a severe shortfall in the number of cadaveric kidneys available for transplantation in the UK and greater use of kidneys from living donors offers considerable scope for increasing the number of transplants performed. The main objection to living kidney donation is that it exposes the healthy donor to the risks of major surgery and life with a solitary kidney. Living donor kidney transplantation must be undertaken with the highest possible standard of clinical care and as part of a

properly planned programme. It is essential to ensure that donor morbidity is kept to an absolute minimum and that transplant outcome is optimised. The potential donor must be fully informed and free from coercion and rigorous assessment must be undertaken to determine their suitability to donate.

A recent survey of renal transplant centres in the UK and Ireland emphasised the wide variability between units in the organisation of living kidney donor evaluation and the method of assessment.<sup>(3)</sup> The authors highlighted the need to establish national guidelines in order to provide consistency in the standard of assessment and care of living donors.

## 1.2 PURPOSE OF THE GUIDELINES

This document provides guidelines on most aspects of living donor kidney transplantation. It also describes standards of clinical care and audit goals for the practice of living donor kidney transplantation in the UK. Particular emphasis is given to the assessment of the suitability of the potential kidney donor and to ensuring that donation is altruistic, without coercion or financial reward and that the risks to the donor are minimised. The guidelines were prepared with the aim of assisting clinicians and other health care workers involved with living donor kidney transplantation. It is hoped that the document will be of value in enabling individual clinicians and hospitals in the UK to produce their own local protocols for living donor kidney transplantation.

The guidelines provided in this document are not meant to be overly prescriptive or to be used as a substitute for clinical experience.

### 1.3 PREPARATION OF THE GUIDELINES

The guidelines were prepared by a working party of the BTS and the Renal Association and are based on consensus and review of the literature (up to December 1999). In a number of areas, knowledge is insufficient to allow definite guidelines to be formulated and in all cases good clinical judgement remains paramount. For many areas insufficient evidence is available to meet the recommendations of the Evidence-Based Medicine Working Group or the National Health Institute guidelines.<sup>(4, 5)</sup> For the same reason the grading of recommendations, as adopted by the Canadian Task Force on the Periodic Health Examination, was not attempted.<sup>(6)</sup>

The membership of the working party is listed in appendix 1 and included transplant surgeons, nephrologists, co-ordinators and a clinical scientist. The group has experience in both adult and paediatric practice. The working party met on four occasions between April 1998 and September 1999. Individual members were allocated responsibility for one or more sections of the document and initial drafts were reviewed by the entire working party. Advice and comments were also received from a number of other individuals (listed in appendix 2) and their contribution is gratefully acknowledged.

The first two listed members of the working party undertook most of the editorial work.

The guidelines have been distributed to all BTS and Renal Association members, directors of renal transplant units, Chief Executives of Acute Trust Hospitals in the NHS and private sector, and are accessible on the world wide web:

<http://www.jr2.ox.ac.uk/bts/index.htm>

Living donor kidney transplantation requires adequate resources to ensure that it is performed to the highest standard and it is important that service contracts reflect the costs for adherence to the guidelines in this document. As new developments in clinical practice occur, the guidelines will require regular updating and the clinical standards will require further refinement.

**This document represents the first step in an ongoing commitment by the BTS and the Renal Association to set standards of clinical care and produce guidelines for living donor kidney transplantation.**

**The guidelines cover most aspects of living donor kidney transplantation with particular emphasis on evaluation of the potential donor.**

**Throughout the document, the endorsements of “Best Practice”, “Standards” and “Summary points” are highlighted.**

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## 2.0 Current status of living donor kidney transplantation

### 2.1 RENAL TRANSPLANTATION

Renal transplantation is the optimal treatment for the majority of patients in end-stage renal failure (ESRF). It improves their quality of life and may also increase long-term survival.<sup>(1-4)</sup> Renal transplantation is also the most cost effective form of treatment for patients in ESRF.<sup>(5)</sup> Unfortunately, the supply of donor organs (cadaver and living donor), which averages only 28 pmp per year in the UK, is greatly outstripped by demand which is 79 pmp.<sup>(6)</sup> Over the last decade there has been a 7-10% annual increase in the UK dialysis population. A steady decline in the number of cadaver kidney transplants performed throughout the 1990s, together with an increasing number of patients on the transplant waiting list has led to a severe shortage of organs for transplantation.<sup>(6)</sup> The decline in the number of cadaveric organ donors in the UK has been attributed, in large part, to the fall in death rates from road traffic accidents and intracranial haemorrhage.<sup>(7, 8)</sup> An additional contributing factor is the shortage of intensive care beds which precludes the admission of some comatose patients with cerebrovascular accidents who, on the basis of modern imaging techniques, have been judged to have a poor prognosis and therefore likely to become organ donors.<sup>(9)</sup>

### 2.2 LIVING DONOR KIDNEY TRANSPLANTATION

Kidneys obtained from living genetically-related and non-related donors have a better outcome than those from cadaveric donors. The use of kidneys from living donors also offers a partial solution to the severe shortage of cadaveric organ donors. A King's Fund Institute report (1994) on the provision of donor organs for transplantation recommended that living donation in the UK should be expanded in an attempt to increase the availability of kidney transplantation.<sup>(7)</sup> The number of living donor kidney transplants performed in the UK has risen over the last decade (Table 2.1) but living donor transplants still represent only around 15% of all renal transplants performed (around four living donor transplants pmp per year). In addition, there is marked variation in the ratio of living to cadaveric donor transplant activity between different transplant units<sup>(6, 10)</sup> suggesting that not all patients in the UK have equal access to living donor transplantation.

**Table 2.1**  
Living donor kidney transplantation in the UK

Year	Number of transplants	
	(Related)	(Unrelated)
1993	119	3
1994	121	1
1995	150	6
1996	177	6
1997	164	11
1998	225	20
1999 (first six months)	99	10

Data from UKTSSA

The number of living donor kidney transplants performed in North America, Australia and in many European countries is substantially higher than in the UK<sup>(11)</sup> (Table 2.2). In Norway 38% (18 pmp per year) of all kidneys are obtained from living donors, and as a result a total rate of 46 transplants pmp per year has been achieved.<sup>(12)</sup> In the USA, living donor transplants account for around 30% of kidney transplants performed.<sup>(13)</sup>

Table 2.2

## Kidney transplantation activity for 1998 (pmp)

	Living	Cadaveric
Norway	18	28
USA (UNOS)	16	35
Sweden	14	27
Greece	8	9
Australia	8	19
Denmark	7	20
Netherlands	7	25
Austria	6	41
Germany	4	25
UK & Ireland	4	24
France	1	31
Italy	1	21
Spain	1	50

Data from Reference 11

In many countries the use of genetically unrelated living donors, such as spouses, unmarried life-long partners, step-parents and even close friends, is becoming widely accepted. The graft survival rates for such transplants are comparable to related living donor transplants and superior to those for cadaver grafts.<sup>(14, 15, 16)</sup> There has been an increase in the number of living unrelated kidney transplants carried out in

the UK although the overall number of such transplants remains very small (Table 2.1).

Most UK transplant centres support the view that there should be a further expansion of living donor transplant activity in the UK, in line with North America and many other European countries. It is likely, therefore, that the number of living related and living unrelated transplants performed in the UK will increase further over the next decade.

*Summary point: Living donor kidney transplantation offers recipients the best hope of long-term rehabilitation. The number of living donor kidney transplants performed annually in the UK (4pmp) is low. There is considerable scope for increasing living donor transplant activity and a target in excess of 10 pmp per year seems reasonable.*

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Living donor kidney transplantation raises a number of important ethical issues and it is essential that the health care professionals involved are fully aware of these when drafting transplant unit policy and deciding whether living donor transplantation can be justified for a particular donor-recipient pair.

### 3.1 JUSTIFICATION FOR LIVING DONOR KIDNEY TRANSPLANTATION

The major concern in living donor kidney transplantation is that it exposes an otherwise healthy individual to the risks of major surgery and life with a single kidney entirely for the physical benefit of another individual. Justification of this requires careful consideration of the risks and benefits to the donor and recipient.<sup>(1)</sup>

Living donor kidney transplantation should only be undertaken if four essential conditions are met. These are:

- The risk to the donor must be low.
- The donor must be fully informed.
- The decision to donate must be entirely voluntary and not due to coercion or the offer of an inducement (see Section 4.0 Legal issues).
- The transplant procedure must have a good chance of providing a successful outcome for the recipient.

### Advantages of living donor kidney transplantation

The advantages of living donor kidney transplantation for the recipient are indisputable: patient and graft survival for living donor transplantation are better than for cadaveric transplantation. This is not attributable to better HLA matching alone since even a poorly matched living donor kidney graft fares better than a well-matched cadaveric graft.<sup>(2, 3)</sup>

Living donor transplantation avoids the long and unpredictable wait for a cadaveric kidney, and the benefits of transplantation are realised more quickly. Pre-emptive transplantation may be possible, thereby avoiding completely the need for dialysis.<sup>(4)</sup> Although kidney donors gain no physical benefit from the transplant procedure, they usually gain psychological benefit in the form of increased self-esteem, knowing that their gift has provided an opportunity to improve dramatically the quality of life of a relative, partner or close friend.<sup>(3, 5, 6)</sup>

A potential donor may also benefit occasionally if an unrecognised and treatable condition is discovered during the rigorous evaluation to determine their medical suitability for donation.

Living donor kidney transplantation has a beneficial effect on the transplant programme overall, since it reduces the number of recipients competing for the limited number of cadaveric organs. However, this alone is not an ethically acceptable argument for promoting living donor transplantation.

### Disadvantages of living donor kidney transplantation

The physical disadvantages of living donor kidney transplantation are borne entirely by the donor. Most important are the possibility of peri-operative mortality and morbidity along with the long-term risks of life with a single kidney; these are considered in detail in Section 5.0. In general for a completely healthy kidney donor the risk of death is extremely low and major complications are uncommon but the physical impact of a successful surgical operation should not be belittled. In addition to the physical risks, living donor transplantation may also impose psychological strains on both the donor and recipient, especially in the presence of unrecognised coercion.

It is important to consider the possibility that placing a prospective living kidney donor in a position where they choose whether or not to be considered as a donor may, irrespective of their eventual decision, have a life-long impact on them. It may affect their relationship with the prospective recipient as well as with other family members. Another disadvantage for the prospective donor is the possibility that the medical assessment will reveal a disease or condition for which there is no effective treatment. The discovery of such a condition may adversely affect the prospective donor's outlook on life and may affect their ability to obtain life insurance. Finally, if the prospective donor is considered suitable and transplantation is undertaken, the donor may suffer

financial disadvantage from lost opportunity during recovery from the donor operation.

Critics of living donor transplantation have argued that it challenges the principle of non-maleficence – “First do no harm.” However, this concern must be set against the right of altruistic and fully informed donors to determine the risks that they are willing to undertake. Moreover, it can be argued that the action of denying a perfectly healthy and informed altruistic donor the right to donate a kidney to a loved one may cause psychological damage.

The extent to which truly informed consent for living kidney donation can be obtained in the context of the emotional relationship with the recipient has also been questioned.<sup>(7-9)</sup> Donors may feel under pressure to donate because of family pressure or through a feeling of guilt at not offering to donate. In one study, 6% of donors thought they were under undue family pressure to donate.<sup>(10)</sup> However, the majority of donors consider donation to be a positive experience. With respect to guilt, Singer *et al* emphasised that the need to balance selfishness and altruism was a normal feature of family life and did not, in their view, invalidate voluntary consent.<sup>(9)</sup> Interestingly, Spital states that the more distant the relationship of the donor to the recipient, the less likely there is to be psychological coercion and the more likely the altruistic donor is to be a true volunteer.<sup>(11)</sup>

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### 3.2 INDIVIDUAL AUTONOMY AND MEDICAL PATERNALISM

A major role of the transplant team is to inform the potential donor of the risks of kidney donation and the likelihood of a successful outcome of the proposed transplant. It is for the healthy, informed, altruistic donor to decide whether the risks of nephrectomy are acceptable. The question arises, however, as to whether the final decision of a well-informed, altruistic potential donor to donate should rest with the transplant team or the donor. This question is especially relevant when there are concerns about the medical suitability of the potential donor and when the chances of a successful outcome after transplantation are reduced because of recipient factors.

The legitimacy of the health care professionals adopting a paternalistic approach that denies a potential donor the opportunity to donate has been the subject of considerable debate. Spital argues that the autonomy of the donor should be respected and promoted over medical paternalism.<sup>(12)</sup> “Whether or not donation makes sense,” he argues “is ultimately a value judgement that should be made by the individual who is most at risk – the competent donor”. The transplant team has a duty to evaluate the risks and advise the donor accordingly but the donor should make the final decision.<sup>(13)</sup> On the other hand it is generally accepted that when a potential donor is judged to be at an unacceptably high risk the transplant centre is fully entitled to decline transplantation.

In such a situation, the health care professionals involved should consider sympathetically the potential donors’ views and explain the reason for refusal. Beauchamp and Childress<sup>(14)</sup> state that “Simply letting prospective donors decide or letting transplant teams decide (assuming the potential donor’s willingness to donate) is inadequate. Both parties should be involved as responsible moral agents in the donation process.” If the potential donor still feels dissatisfied with the final decision they should be offered the option of referral for a second opinion.

*Best Practice: The transplant team should respect the autonomy of the prospective donor. The team has a duty to evaluate the risks of donation and the likely success of transplantation and inform the donor and, where appropriate, the recipient accordingly. Transplantation should only be undertaken if the transplant procedure has a good chance of success, the risk to the donor is low and donation is entirely voluntary.*

### 3.3 UNRELATED LIVING DONOR KIDNEY TRANSPLANTATION

Until quite recently living donor kidney transplantation, at least in the UK, was limited almost exclusively to donors who were genetically related to the recipient. The traditional medical view is that the best donor is a member of the recipient’s immediate family. However, living donor kidney transplants between genetically unrelated donors also fare better than predicted and the results for unrelated

living donor transplantation are very similar to those for living donor transplants matched for one Human Leucocyte Antigen (HLA) haplotype.<sup>(3)</sup>

Emotionally related donors, like genetically related donors, usually gain increased self-esteem and benefit from the improved quality of life of their loved ones.<sup>(3)</sup> The risks to the donor are, of course, identical irrespective of whether or not they are genetically related to the recipient. There is, therefore, no ethical reason why a donor with a strong and enduring emotional relationship with the proposed recipient such as a spouse, an adoptive parent or a close friend should not be considered as a potential living donor.

There has been a marked rise in living unrelated donor transplantation recently, the majority of which are between spousal donor-recipient pairs.<sup>(3)</sup> Public opinion in the USA suggests that a majority of the population (88%) would be willing to donate to their spouses and many individuals (66%) would also consider donating a kidney to a close friend.<sup>(11, 12)</sup>

*Summary point: The results of living unrelated donor kidney transplantation are as good as the results for one HLA haplotype matched living related donor transplants. It is ethically acceptable to consider a spouse, an adoptive parent or a close friend (where there is a strong and enduring emotional relationship), as a potential kidney donor.*

### 3.4 ALTRUISTIC STRANGERS

In recent years there has been discussion in the literature about the possibility of accepting a completely unrelated, competent and fully informed volunteer or altruistic stranger as a living kidney donor.<sup>(15)</sup> Offers by altruistic strangers are often regarded indicative of psychological disturbance although there is little evidence to support this view and it is difficult to argue for dismissing such a donor on ethical grounds alone.<sup>(16)</sup> This type of living donor transplant has not been undertaken in the UK.

### 3.5 EXCHANGE DONORS BETWEEN PAIRS OF SPOUSES

In the case of spousal donor kidney transplantation, ABO blood group incompatibility excludes around 30-40% of potential donors from donating to their spouse.<sup>(2)</sup> Exchange donation between pairs of spouses has been suggested as a possible solution to this problem,<sup>(17)</sup> although the number of spouses who could benefit from paired exchange is severely limited, on the basis of blood groups, to around 3%.<sup>(2)</sup> In addition to the practical difficulties raised by paired exchange there are also significant ethical and legal concerns.<sup>(18)</sup> Paired exchange seems, at present, an unlikely development in the UK and may be illegal under the Human Organ Transplant (HOT) Act (1989) because of the clause of “non-coercion”.

### 3.6 THE CHILD OR YOUNG PERSON AS A LIVING DONOR

The ethical concerns about subjecting children to donor nephrectomy are such that individuals under the age of 18 years should rarely, if ever, be considered as potential living donors. Most kidney transplant centres in the USA regard age less than 18 years as an absolute exclusion criterion for donation.<sup>(19)</sup> Some regard the use of an identical twin as an acceptable child donor, on the basis that the outcome for the recipient twin is exceptional and because the relationship between identical twins is so close that restoring the health of the recipient confers major psychological benefit for the donor. The importance of such psychological benefit has, however, been challenged<sup>(20)</sup> and the use of a child donor even for identical twin transplantation remains highly controversial.

In England and Wales the legal position regarding the age of consent for medical treatment was clarified by the Gillick case.<sup>(21)</sup> This determined that minors who are able to understand fully what is proposed and are capable of making a choice in their best interest could give medical consent irrespective of their age. However, even in the case of a “Gillick competent” minor where there is parental consent for donation, it would be advisable to seek consent from the High Court before proceeding. The British Medical Association considers that “it is not appropriate for live, non-autonomous donors (minors) to donate non-regenerative tissue or organs”.<sup>(22)</sup>

No clinician could safely rely on parental consent on behalf of a child too young to understand the nature, purpose and possible consequences of what is involved.

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

### 3.7 THE BTS ETHICS COMMITTEE

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

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The Human Organ Transplant Act 1989 (HOT Act)<sup>(1)</sup> and associated Regulations (1989 and 1998)<sup>(2-4)</sup> set out the legal framework governing living donor renal transplants. Health care professionals involved in living donor transplantation should be fully aware of the requirements placed on them by the HOT Act and by the associated Regulations. The HOT Act<sup>(1)</sup> prohibits commercial dealings in human organs and restricts the transplantation of organs between persons who are not genetically related. The associated Regulations (1989 & 1998):

- Provide for the establishment of The Unrelated Live Transplant Regulatory Authority (ULTRA).<sup>(2)</sup> (See [www.doh.gov.uk/ultra.htm](http://www.doh.gov.uk/ultra.htm))
- Require the registered medical practitioners responsible for removing and transplanting organs to supply specified information to the South West Regional Health Authority.<sup>(3)</sup> The statutory record of this information is held and administered on behalf of the South West Regional Health Authority by UKTSSA.
- Require that a claimed genetic relationship be established by a person approved by the Secretary of State as competent to specify and interpret the results of genetic tests (based on DNA variations).<sup>(4)</sup> If the “Tester” is not satisfied that the claimed genetic relationship between donor and recipient is established, the transplant team is required to seek approval from ULTRA before proceeding.

For the purpose of the HOT Act, a person is genetically related to:

- Their natural parents and children.
- Their brothers and sisters of the whole or half blood.
- The brothers and sisters of the whole or half blood of their natural parents.
- The natural children of their brothers and sisters of the whole or half blood or of the brothers and sisters of the whole or half blood of either of their natural parents.

It should be noted that a person is not, for the purpose of the HOT Act, genetically related to their natural grandparents or grandchildren.

An application must be made to ULTRA when:

- A claimed genetic relationship is outwith that specified in the HOT Act.
- A claimed genetic relationship cannot be confirmed by genetic tests (e.g. when an insufficient number of other members of the family are available for testing).
- The donor and recipient are known not to be genetically related.

Information on how to make a submission to ULTRA and guidance on the manner in which applications should be made, together with the content of such applications, are given in the document *ULTRA – Guidance for Clinicians*.<sup>(5)</sup>

Applications to ULTRA must be made by the clinician who has responsibility for the prospective kidney donor. It is an offence to undertake a transplant between living persons who are not genetically related (as defined in the HOT Act) unless ULTRA is satisfied that the legal requirements specified in the HOT (Unrelated Persons) Regulation 1989 have been met.<sup>(2)</sup> One of the requirements is that the prospective donor and recipient have both been interviewed by a suitably qualified person (independent third party) who has provided a report to ULTRA that (in the context of kidney donation) includes information on the following:

- That a registered medical practitioner has given the prospective donor an explanation of the nature of the medical procedure for, and the risk involved in the removal of a kidney.
- That the prospective donor understands the nature of kidney donation and the risks involved and consents to the procedure.
- That the donor's consent for kidney donation was not obtained by coercion or the offer of an inducement.
- That the donor is free to withdraw consent at any time prior to the transplant operation.
- Any difficulties of communication with the donor and recipient and an explanation of how any such difficulties were overcome.

Although it is illegal to offer, give or receive any payment or other benefit for providing a kidney for transplant, donors may be reimbursed for loss of earnings and other expenses, e.g. travelling and subsistence, which are related to the medical evaluation and kidney donor operation.

Hospital trusts and health authorities are permitted to reimburse the donor for expenses incurred but are under no obligation to do so. However, it seems reasonable that the health authority paying for the recipient operation should also meet the necessary costs incurred by the donor.

*Summary point: It is illegal to undertake a living donor transplant in the UK unless (a) the claimed genetic relationship between donor and recipient falls within that specified in the HOT Act and has been established by an approved tester OR (b) ULTRA has given approval for the transplant to proceed.*

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2. The Human Organ Transplants (Unrelated Persons) Regulations 1989. HMSO. ISBN 0 11 09848 3.
3. The Human Organ Transplants (Supply of Information) Regulations 1989. HMSO. ISBN 0 11 098108 1.
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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.

### 5.1 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.<sup>(1-4)</sup> These studies are retrospective and the data may not be complete. The reported death rates range from 0.03% – 0.06%, the most common causes of death being pulmonary embolus, hepatitis and cardiac events (myocardial infarction and arrhythmias).<sup>(2, 5, 6)</sup> 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%).<sup>(4)</sup> There have been at least two peri-operative donor deaths in the UK.<sup>(7)</sup> One was due to myocardial infarct and one to pulmonary embolus.

*Summary point: The peri-operative mortality rate for living donor nephrectomy is reported at 1 in 1,600 to 1 in 3,300.*

### 5.2 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 peri-operative complication rates for living donor nephrectomy have been summarised for a large number of single centre studies.<sup>(4)</sup> The mean overall complication rate was 32% and the major peri-operative complication rate was 4.4%. The estimated 'major complication' rate in a survey by Bay and Hebert<sup>(3)</sup> was 1.8% whereas the American Society of Transplant Physicians (ASTP) survey<sup>(1)</sup> reported that 22 out of 9692 (0.23%) kidney donors experienced 'potentially life-threatening or permanently debilitating' complications.

Kasike *et al*<sup>(4)</sup> extracted data from a large number of published reports and calculated the reported rate (mean and SD) for specific complications. These are shown in Table 5.1.

**Table 5.1**  
Complications after donor nephrectomy

Complication	Frequency (mean and s.d.)
Pneumonia or atelectasis	9.3% ± 10.8%
Pulmonary atelectasis	7.4% ± 10.8%
Urinary tract infection	5.3% ± 6.3%
Wound infection	4.3% ± 5.5%
Pneumothorax	3.1% ± 4.1%
Urinary retention	1.0% ± 2.2%
Ileus	1.0% ± 2.1%
Pleural effusion	0.9% ± 1.8%
Intra-abdominal haematoma	0.5% ± 1.2%
Pulmonary embolus	0.4% ± 0.8%
Wound herniation	0.3% ± 0.7%
Wound haematoma	0.3% ± 0.7%
Splenectomy	0.2% ± 0.5%
Deep venous thrombosis	0.2% ± 0.6%
Intra-abdominal abscess	0.2% ± 0.7%
Other unspecified	5.3% ± 6.8%

Data from Reference 4.

It is important to note that many of the studies quoted above were undertaken over a decade ago. In a recent single centre report of 871 kidney transplants performed between 1985 and 1995, only two patients experienced a major complication (femoral nerve injury and a retained sponge requiring reoperation).<sup>(8)</sup> 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 transperitoneal approach. Irrespective of the type of incision, wound pain is a major source of anxiety for the donor.

Modern approaches to post-operative pain limit but do not completely prevent post-operative wound pain. A small number of patients develop prolonged wound discomfort, which may require referral to a pain clinic. The precise incidence of prolonged wound pain is difficult to determine but the figure of 3.2% reported by Cosimi<sup>(9)</sup> should be regarded as realistic.

*Summary point: The major peri-operative complication rate for donor nephrectomy is approximately 2%.*

### 5.3 LONG TERM RISKS

There is a need for more detailed long-term follow-up data on living kidney donors but a substantial body of published evidence indicates that there is little long-term medical risk after unilateral nephrectomy in a healthy donor.

#### 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. The first is the experience of children and young adults who have undergone unilateral nephrectomy: the children principally for tumour<sup>(10)</sup> and the young adults because of trauma in World War 2.<sup>(11)</sup> 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 world-wide 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.<sup>(12)</sup> 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”.

### Development of Hypertension

There is no convincing evidence that unilateral nephrectomy significantly increases the risk of hypertension. Hypertension is a common problem in the general population and the prevalence varies markedly between countries. The reported incidence of hypertension after kidney donation ranges from 9% in Turkey to 45% in the UK.<sup>(12-19)</sup> 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 studies do suggest that hypertension is more common after kidney donation. In one such study, 29 kidney donors from the USA were followed for between nine and 18 years, and the incidence of hypertension was found to be higher than expected after adjustment for age, sex and race.<sup>(20)</sup> Another North American report on 52 donors, followed for at least ten years in the male (but not female) cohort, reported an increase in hypertension compared to matched outpatient control subjects.<sup>(21)</sup>

Similarly, a longitudinal study of 47 kidney donors in the USA reported an increase in the prevalence of hypertension compared to age and sex matched controls from the general population.<sup>(22)</sup>

On the other hand, two North American studies compared the incidence of hypertension in kidney donors to that in their siblings and found no difference in the (very high) incidence of hypertension between the groups.<sup>(2, 23)</sup> These studies followed 38 and 57 donors for more than ten and 20 years respectively. Furthermore a meta-analysis of 48 studies involving 3,124 patients 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.<sup>(24)</sup>

### Proteinuria

Asymptomatic proteinuria is common after unilateral nephrectomy. A small increase in proteinuria has been reported in up to a third of kidney donors.<sup>(2, 13, 16, 17, 18, 20, 21, 22, 24, 25)</sup> However, the level of proteinuria is generally mild (less than 0.5 g/24 hours), is not progressive and has no adverse effects on the health of the donor.

### Renal Function

Some authors, using serial measurement of serum creatinine as a measure of renal function, have reported no change after uninephrectomy.<sup>(14, 15, 27)</sup>

Others, using serial serum creatinine measurements prior to and at intervals after kidney donation, have reported a small increase in the function of the residual kidney after donor nephrectomy.<sup>(13, 16)</sup> Serial creatinine clearance estimation in 46 donors showed long-term renal function was, on average, 78% of the pre-nephrectomy value.<sup>(18)</sup> When Glomerular Filtration Rate (GFR) is measured by DTPA<sup>(27)</sup> or inulin clearance as well as creatinine clearance,<sup>(20)</sup> long-term renal function is approximately 73-85% of that observed in age, sex and race matched controls. The rate of decline in GFR after donor nephrectomy appears to be consistent with the normal age-dependent decline in renal function.<sup>(12, 17)</sup>

Isolated cases of end stage renal failure in kidney donors have been reported despite satisfactory evaluation of renal function prior to donation.<sup>(16, 29, 30, 31)</sup> A survey of North American units carried out by the ASTP revealed 15 donors with renal impairment, of whom 11 were on dialysis.<sup>(1)</sup> 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 disease in the donor population overall is less than that seen in the general population.

*Summary points:*

- Donors who successfully complete the evaluation for living kidney donation have an above average life expectancy.
- Prospective donors who are normotensive are probably at no higher risk of developing hypertension than the general population.
- Around 25-35% of donors develop asymptomatic, non-progressive proteinuria.
- After unilateral nephrectomy, compensatory changes occur in the remaining kidney. Donors have approximately 75% of normal renal function, which declines normally with age.
- The risk of developing dialysis dependent renal failure after kidney donation is less than that of the general population.

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The General Medical Council (GMC) is explicit about the responsibility of registered doctors when seeking informed consent.<sup>(1)</sup> Central to the validity of the process is respect by the medical practitioner for the right of the individual to exercise autonomy and the provision of information in a form that allows them to make an informed decision.

### 6.1 INFORMED CONSENT FOR LIVING KIDNEY DONATION

The need for informed consent should be explained to the potential donor and they should be provided with information on the implications of kidney donation in both verbal and in written form. The mortality of living donor nephrectomy and the risk of short and long-term complications should be fully explained. In addition, 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 should be discussed openly with the potential donor.

Consent must be freely given and it is essential that the consenting clinician 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.

The option for a potential donor to withdraw with dignity at any stage in the preparation for donation, without having to provide an explanation for their action, must be made clear from the outset and they must be allowed adequate time to reflect on their decision to donate.

The decision to donate a kidney to another person can generate a significant amount of stress to both parties and involve family members, partners and friends. (See also Section 3.1).

Occasionally several family members may initially be contemplating donation and the decision making, as to who should be considered as the preferred potential donor, may be a complicated and difficult process. Many factors influence this decision and there is a need for the health team involved to provide a sound knowledge base for the process in order that the individuals concerned – both donor and recipient – can make as fully informed decision as is possible.

The prospective donor should be given a balanced view of the advantages and disadvantages of living donor transplantation. They should not be actively persuaded to proceed. Inevitably, some potential donors will decide, after discussion, not to proceed and their decision should be respected. If the donor decides not to proceed, the transplant team should regard this as a natural result of the informing process and not as a failure.

### 6.2 POTENTIAL DONORS WITH POOR USE OF ENGLISH

The provisions of the HOT Act are specifically designed to prevent abuse in this area, but the potential for coercion still exists.<sup>(2)</sup> There is particular concern with respect to 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. In this event, the translator should be unknown to both the donor and recipient. The translator must be competent to discuss the implications and associated risks of donor nephrectomy and the post operative recovery process. They should 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.

### 6.3 THE INDEPENDENT THIRD PARTY

In the case of unrelated living donor kidney transplantation it is a requirement of The Human Organ Transplants (Unrelated Persons) Regulations 1989<sup>(3)</sup> that the prospective donor and recipient are interviewed separately by an independent third party to ensure that the conditions contained in the Regulations are met. The independent third party is generally an NHS consultant physician, surgeon or psychiatrist, or someone of equivalent professional status, who is not otherwise party to the transplant proceedings nor a close associate of one who is.<sup>(4)</sup> The third party should not be

practising in the field of renal medicine or renal transplantation. They are required to report as specified in Section 4.0.

In the case of living related donors (as defined by the HOT Act,<sup>(2)</sup>) there is no legal requirement for a third party opinion. However, in 1992 the GMC issued guidance on transplantation of organs from live donors (<http://www.gmc-uk.org>) stating that “a doctor, or another appropriately qualified professional, independent of the transplant team, must assess the motivation of each donor.” The GMC guidance further states that “the doctor responsible for the medical care of the recipient should not at the same time assume sole responsibility for the medical care of the donor and in particular should not assess the motivation and medical suitability of the donor.” This approach ensures maximum protection of the donor’s interests.

All living related donors should be offered the opportunity to discuss the situation with an independent health care practitioner or “donor advocate” who has a good understanding of the issues relating to living kidney donation. Such a person could be a physician, family GP, psychiatrist or counsellor.

#### 6.4 PSYCHOSOCIAL ISSUES

The assessment of the prospective donor should include an evaluation of their state of psychological well being. The doctor caring for the donor is responsible for informing them of the potential psychosocial after-effects of kidney donation. These may include depression, guilt, financial difficulty and relationship problems.<sup>(5, 6)</sup> Overall, however, psychological problems after donation are usually minor.<sup>(5, 7)</sup> An independent assessment of the psychosocial implications for the donor may be helpful and may uncover previous psychiatric disorders, psychological problems and perhaps, most importantly, covert pressures to donate.<sup>(8)</sup> In many transplant centres a designated person (usually a transplant co-ordinator or nurse practitioner) plays a key role in organising the medical assessment of the prospective donor. During the assessment, such individuals generally become closely acquainted with the donor and their family and are able to provide the support needed by the donor and recipient and relevant family, partners or friends. Some transplant centres have social workers or psychologists associated with them and are able to refer appropriately when necessary.

Prospective donors should be alerted to the need to check with their insurance companies to confirm that they will not be disadvantaged with respect to mortgage and life insurance, if they undergo medical work-up and donate a kidney.

Donors usually maintain their high esteem in the event of transplant rejection or failure, although it should be recognised that regret, guilt and diminished closeness to the recipient may occur.<sup>(9, 10)</sup> In this eventuality, continuing support should be provided to the donor by a relevant health care professional. Bratton<sup>(11)</sup> recommends that assistance in the form of independent counselling or support should also be made available to the potential donor who makes a final decision not to donate a kidney.

#### 6.5 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.<sup>(1)</sup> It is recommended that a combination of verbal and written information is given to potential donors and that the areas listed in Table 6.1 are specifically addressed.

**Table 6.1**  
**Areas to be covered when discussing the potential risks of donor nephrectomy**

1. The risk of death (estimated to be approximately 1 in 1600-3300 cases).
2. Idiosyncratic reaction to anaesthetic or other drugs.
3. The general complications of major abdominal surgery.  
 Specific mention should be made of:
  - a) Venous thromboembolism (deep vein thrombosis and pulmonary embolism)
  - b) Intra-abdominal bleeding and abscess formation
  - c) Wound complications (haematoma, infection and herniation)
  - d) Chest complications (pneumothorax, pneumonia and atelectasis)
  - e) Urinary retention/ urinary tract infection
  - f) The possible need for blood transfusion
  - g) The risk of adhesive small bowel obstruction (after transperitoneal nephrectomy)
4. The possibility of short and long-term wound pain.
5. The need for a recovery period of between 4-12 weeks after surgery. Potential donors should be advised to check their entitlement to paid sick leave with their employers.
6. The possibility that kidney donation may in the long term lead to a small increase in blood pressure and is associated with an increased incidence of proteinuria.
7. The possible psychological after-effects of kidney donation.
8. The psychological impact on the donor of premature transplant failure.
9. The need to check the implications of donation with their insurance agency.

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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. Absolute and relative exclusion criteria for living donation are listed in Table 7.1.

In order to avoid important omissions, the evaluation of potential donors should be carried out according to a well-rehearsed protocol. Investigations should be undertaken in a logical sequence so that the potential donor is protected from invasive procedures, such as an angiogram, until there is a reasonable certainty that donation will proceed. There is good agreement regarding the routine screening tests that should be performed.<sup>(1,2,3)</sup>

Throughout the evaluation, it is important to maintain good communication with the GP caring for the potential donor.

The stage during the donor evaluation at which to remove a recipient from the waiting list for a cadaveric kidney will vary according to individual circumstances and preference and should be decided after discussion with individual donor and recipient pairs.

Evaluation of potential living donors is an expensive and time consuming 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.

**Table 7.1**  
Exclusion criteria for living kidney donor transplantation.

Absolute contraindications	Relative contraindications
Inability to give informed consent	Age below 18 years (but able to give informed consent)
Evidence of coercion	Age over 70 years
Hypertensive end-organ damage	Intellectual impairment but able to give informed consent
Body mass index >35 kg/m <sup>2</sup>	Obesity: body mass index of 30-35 kg/m <sup>2</sup>
Most malignancies	Cigarette smoking
Pregnancy	Risk factors for Type 2 diabetes mellitus
Intravenous drug abuse	Females of child bearing age
HIV or HTLV infection	Psychiatric disorder
Major respiratory or cardiovascular disease	Hepatitis B infection
Other major co-morbid illness	History of deep vein thrombosis or pulmonary embolism
Thrombophilia	Hypertension
Diabetes mellitus or impaired glucose intolerance	Renal tract abnormality
Renal disease	
Systemic disease affecting kidneys	

Evaluation of the living donor can be conveniently divided into 5 phases:

**1. ABO blood grouping and crossmatch testing**

ABO blood grouping allows the early identification of individuals who cannot donate because of ABO blood group incompatibility.<sup>(4)</sup> It may be undertaken by the GP, or at a renal transplant assessment clinic. After blood group compatibility has been established, initial HLA typing and crossmatch testing should be performed (See Section 18.0).

**2. A complete medical assessment**

This may reveal previously undiagnosed disease and it is important to warn potential donors of this possibility. The existence of a previously unrecognised condition may, for example, prejudice future attempts to obtain life insurance.

A full medical history must be taken and the areas listed in Table 7.2 should be specifically addressed. 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 (Table 7.3; also Section 17.0).

A rigorous clinical examination must be performed, taking particular account of the cardiovascular and respiratory systems and including the assessments listed in Table 7.4.

As noted in Section 6.0, the doctor responsible for the medical care of the recipient should not at the same time assume responsibility for assessing the medical suitability of the potential donors.<sup>(5)</sup>

In the ideal situation, a physician or surgeon who does not also have direct responsibility for the transplant recipient should undertake medical evaluation of the potential donor<sup>(5)</sup>. It is accepted, however, that this is not always necessary or, for logistic reasons, possible.

After obtaining the history and physical examination it is appropriate to initiate the routine screening investigations listed in Table 7.5.

**Table 7.2**  
Points of particular importance when obtaining the medical history of a potential kidney donor

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Haematuria/oedema/urinary tract infection
Nephrolithiasis
Gout
Ischaemic heart disease
Cardiovascular risk factors
Hypertension
Diabetes mellitus
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
Family history of diabetes
Smoking
Problems with alcohol or drug dependence
Psychiatric history
Obstetric history
Residence abroad
Previous medical assessments for life insurance

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**Table 7.3**  
**History with respect to transmissible infections**

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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

High risk of HIV, HTLV1 and HTLV2 infection

- Drug addicts
- Sexual partner of drug addict
- Female sexual partner 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 within the last 2 years of an indigenous African
- Homosexuals
- Haemophiliacs and their sexual partners

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**Table 7.4**  
**Points of particular importance when undertaking clinical examination of potential kidney donors**

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Body mass index

Blood pressure measurement (3 times in 10 minutes)

Examination of the cardiovascular and respiratory system

Examination for abdominal masses or hernia

Examination for lymphadenopathy

Examination of the breasts

Examination of the testes

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**Table 7.5**  
**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**

- Haematological profile
- Haemoglobin and blood count
  - Coagulation screen (PT and APTT)
  - G6PD deficiency (where indicated)
  - Sickle cell trait (where indicated)
  - Haemoglobinopathy (where indicated)

**Biochemical profile**

- Creatinine, urea and electrolytes
- Liver tests (including Alanine Transaminase)
- Bone profile (calcium, phosphate, albumin and alkaline phosphatase)
- Fasting plasma glucose
- Glucose tolerance test (if fasting plasma glucose 6-7 mmol/l)
- Urate
- Thyroid function tests (if strong family history)
- Pregnancy test (if indicated)

**Virology and infection screen**

- 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)
-

**3. Assessment of renal anatomy**

The renal anatomy should be assessed to confirm the presence of two kidneys of normal size and to identify abnormalities such as a duplex collecting system, hydronephrosis, pelvo-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.<sup>(2, 6)</sup>

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.

**4. Assessment of renal function**

Accurate measurement of renal function in a prospective donor is important for ensuring adequate residual kidney function in the donor, as well as sufficient graft function in the recipient following transplantation.

An assessment of glomular filtration rate (GFR) should be made in all potential donors. Serum creatinine is often used as a surrogate marker for renal function and simple formulae have been derived to calculate the GFR based on the serum creatinine concentration. For example, the Cockcroft-Gault equation<sup>(7)</sup> is widely used:

$$\text{GFR (ml/min)} = \frac{(140 - \text{age}) \times \text{ideal body weight (Kg)}}{0.8 \times \text{serum creatinine } (\mu\text{mol/l})}$$

(15% less in females)

However, this approach is not sufficiently accurate for assessing renal function in a prospective donor. Measured creatinine clearance, if performed correctly, provides a satisfactory assessment of renal function but caution is required since timed urine collections are susceptible to considerable inaccuracy. Table 7.7 shows the mean and lower limit (mean – 2 SD) of creatinine clearance according to age range.

**Table 7.7 Renal function as determined by creatinine clearance according to age range**

Age range of subjects (years)	Number of subjects	Mean creatinine clearance ml/min/1.73m <sup>2</sup>	Standard deviation	Mean minus two standard deviations
17-24	10	140	11.7	117
25-34	73	140	21.4	97
35-44	122	133	20.0	93
45-54	152	127	17.3	93
55-64	94	120	16.5	87
65-74	68	109	16.5	76

Adopted from Reference 8

**Table 7.8 Renal function as determined by inulin clearance according to age range**

Age range of subjects (years)	Number of subjects	Mean inulin clearance ml/min/1.73m <sup>2</sup>	Standard deviation	Mean minus two standard deviations
24-29	9	123	16.4	90
30-38	9	115	10.8	93
40-49	10	121	23.3	74
51-59	11	99	14.6	70
61-68	10	96	25.5	45
70-78	9	89	19.9	49

Adopted from Reference 9

A creatinine clearance of 80 ml/min/73m<sup>2</sup> is a reasonable lower limit for kidney donation. Radioisotopes, such as <sup>51</sup>Cr EDTA, provide a more reliable measure of GFR since they are not dependent on the accuracy of a timed urine collection. Table 7.8 shows the mean and lower limit (mean – 2SD) for GFR (measured as inulin clearance) for different age ranges. Isotopic methods also provide a measurement of divided renal function. This information is advisable before nephrectomy and especially important if anatomical investigations have shown one kidney to be significantly smaller in size. 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.

It is difficult to recommend a minimum GFR but a value of >70ml/min/1.75m<sup>2</sup> is desirable to ensure that the recipient renal function remains adequate as the GFR declines naturally with age (by around 10 ml/min/decade after the age of 40 years).<sup>(9)</sup> After unilateral nephrectomy the GFR in the donor recovers to around 75 percent of that prior to donation.

*Best Practice: In addition to serum creatinine, GFR should be measured as clearance of creatinine or of an isotopic marker: a prospective donor should not be considered further if the GFR is less than 2SD below the mean. It is difficult to recommend a minimum GFR but in general a GFR of 70ml/min/1.75m<sup>2</sup> is desirable.*

### 5. Definition of the 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.<sup>(10)</sup> 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,<sup>(11,12)</sup> but

do not adversely influence recipient or graft survival.<sup>(13)</sup> It may be acceptable to use a kidney with multiple renal arteries for transplantation, provided 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. 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 catheterisation.<sup>(14)</sup> 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.<sup>(15)</sup> The reported rate for minor complications is 1-5% and the most common problems are haematoma and prolonged bleeding from the puncture site.

Spiral computed tomographic angiography (spiral CTA) and gadolinium-enhanced magnetic resonance angiography (MRA) are relatively new techniques for vascular imaging which are currently being assessed

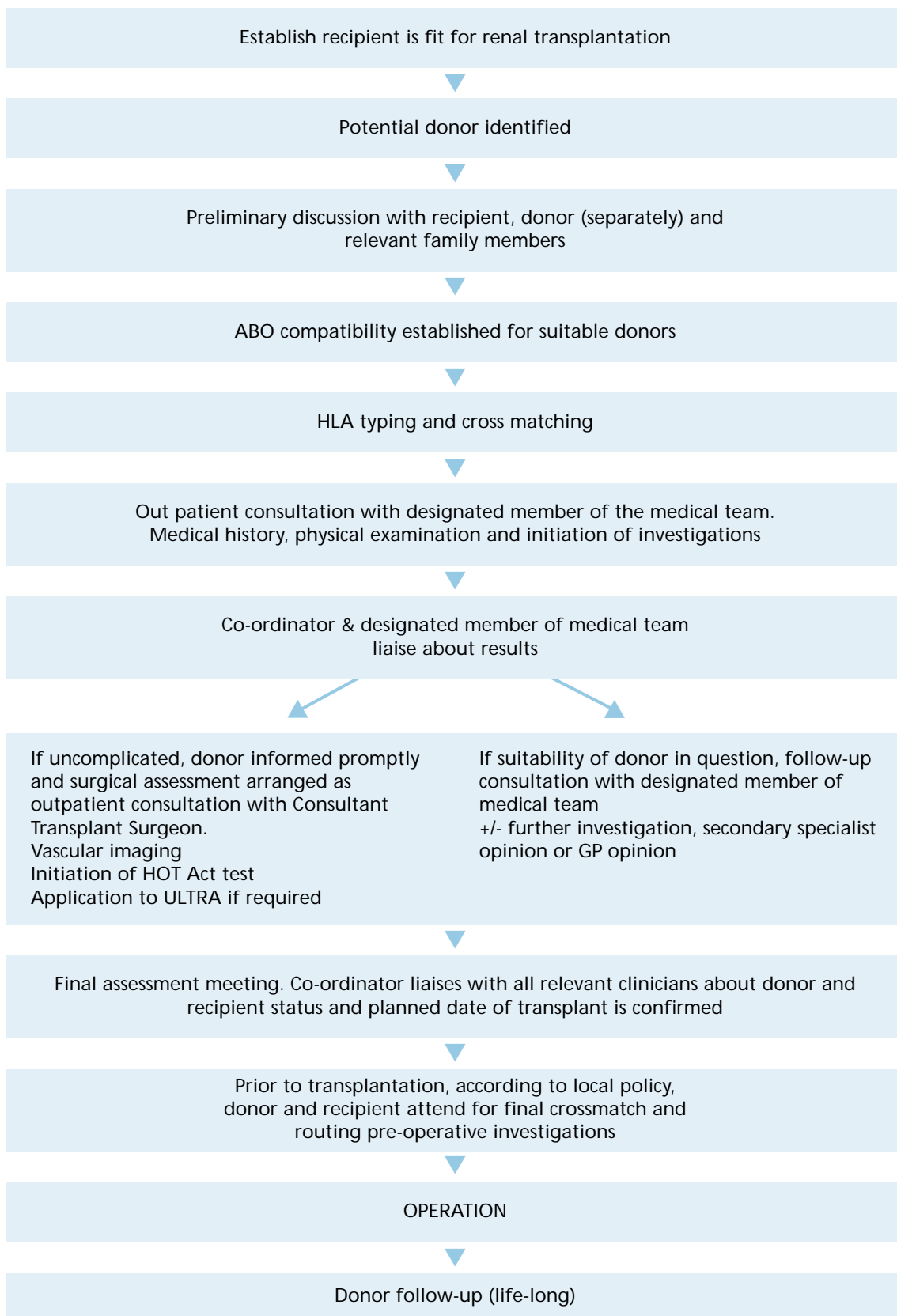
as alternatives to conventional angiography for the preoperative evaluation of donor vascular anatomy. Experience so far is relatively limited but early studies suggest that both CTA and MRA are as accurate as conventional intra-arterial digital subtraction angiography for defining renal arterial anatomy.<sup>(16-18)</sup> It should be noted, however, that accessory polar renal arteries may be missed by all current imaging techniques. The newer imaging modalities are less expensive and can be performed more quickly than conventional angiography. A particular advantage of MRA is that it avoids exposure to radiation. In the case of spiral CTA the pelvicalyceal system and ureteric anatomy is also imaged thereby avoiding the requirement for an IVU or renal ultrasound. Spiral CTA can be used to create a three dimensional reconstruction of the renal anatomy and this is likely to prove helpful to surgeons performing laparoscopic donor nephrectomy. In this situation the preoperative identification of posterior lumbar tributaries of the renal vein is very helpful.

*Summary point: Conventional arteriography has a high level of accuracy but carries a small but appreciable risk. Spiral CTA and MRA are non-invasive and are an attractive alternative if they are available. On the basis of a normal renal angiogram, spiral CTA or MRA, the left kidney is usually selected for donation because the longer renal vein facilitates implantation.*

*Best Practice:*

- *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.*
- *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 work-up rather than the specific manner in which it is conducted. The following (Figure 7.1) is a suggested model for donor evaluation.*

Figure 7.1 A model for the organisation of donor assessment



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## 8.0 Donor age

The young and the old each raise different issues with respect to consideration as potential living kidney donors.<sup>(1)</sup> The ethical barriers to the use of minors and young people as living donors are addressed in Section 3.6.

For older donors there are two issues to be considered. First, increasing age may be associated with more post-operative complications after nephrectomy. Johnson *et al* reported no increase in the incidence of post-operative complications when older donors were used.<sup>(2)</sup> 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.<sup>(3)</sup> 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.

The second concern regarding the older donor is the suggestion that kidneys obtained from older living donors have a worse outcome after transplantation.<sup>(3)</sup> Renal function declines progressively with age and kidneys from older living donors have reduced function.<sup>(4)</sup> 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.<sup>(5-7)</sup> 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.<sup>(7)</sup> Another recent study found that in the absence of acute rejection kidneys from older living donors fared as well as those from younger donors.<sup>(8)</sup>

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 compelling evidence for excluding donation on the basis of chronological age alone.<sup>(2, 9, 10)</sup>

*Best Practice: Old age alone is not an absolute contraindication to donation but the medical work-up of older donors must be particularly rigorous to ensure 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.*

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## 9.0 Donor obesity

The prevalence of adult obesity (defined as a body mass index (BMI) of  $\geq$  to 30 kg/m<sup>2</sup>) in England has increased markedly in recent years: 16% of men and 17% of women are classified as obese.<sup>(1)</sup> Obesity is generally considered to be at least a relative contraindication to living kidney donation. It is an independent risk factor for cardiovascular disease, respiratory insufficiency, and diabetes mellitus.<sup>(2-4)</sup> Obese patients are at increased risk from peri-operative complications during and after major surgery, particularly venous pulmonary embolism, respiratory complications and wound infection.<sup>(5, 6)</sup>

In the context of living kidney donation, the presence of obesity may make the donor operation more difficult to perform safely. There is relatively little information on the influence of obesity on the peri-operative complication rate in living kidney donation. A recent single centre study compared the outcome of 107 obese living donors (BMI  $\geq$  27 kg/m<sup>2</sup>) with 116 non obese donors (BMI < 27 kg/m<sup>2</sup>).<sup>(7)</sup> The overall peri-operative complication rate was significantly higher in the obese donors (17% versus 3%). The majority of complications were wound related. Interestingly, in another recent single centre report of 871 donor nephrectomies, a BMI of >30 kg/m<sup>2</sup> was not a significant independent risk factor for peri-operative complications.<sup>(8)</sup>

In addition to the short term risks, obesity will, in the long term, also compound the risk of hypertension (Section 10.0) and diabetes (Section 11.0) in the donor.

*Best Practice: A body mass index (BMI) of more than 35 kg/m<sup>2</sup> should be regarded as an absolute contraindication to kidney donation and a BMI of more than 30 kg/m<sup>2</sup> a relative contraindication.*

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

## 10.1 DEFINITION OF HYPERTENSION

The morbidity for cardiovascular disease increases with blood pressure values that are still within the “normal range”. In normal clinical practice clinicians are usually interested, therefore, in a definition of hypertension such that any morbidity associated with anti-hypertensive treatment is outweighed by the benefit accruing from successful therapy. However, in the context of evaluating a potential living kidney donor this is not the key issue. Hypertension is common following nephrectomy and the need is to ensure that the blood pressure is such that the potential long-term morbidity associated with uninephrectomy is minimised.

One approach is to define an arbitrary level of blood pressure above which all adults are labelled as hypertensive. A threshold of 140/90 mmHg is one such recommendation.<sup>(2)</sup> For individuals who are not diabetic and in whom there is no evidence of cardiovascular disease or target organ damage, both the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure<sup>(3)</sup> and the recently published British Hypertension Society guidelines<sup>(4)</sup> recommend treatment 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. Because blood pressure rises naturally with age, an age and gender related threshold may be appropriate.<sup>(5, 6)</sup> In older donors a systolic blood pressure greater than the threshold of 140 may be considered acceptable.

The large population surveys relating cardiovascular morbidity to blood pressure have relied on “office” measurements. If an individual demonstrates hypertension that settles after five minutes rest then it is reasonable to attribute the initial hypertension to an “alert reaction” and not reject for further assessment.<sup>(7)</sup>

The utility of 24-hour ambulatory blood pressure monitoring in the context of evaluating a living donor is not established, although it is commonly performed. A meta-analysis of 23 studies including 3476 normal subjects provides values for the upper limit of normal defined as the mean plus two standard deviations as follows: 139/87 mmHg for the whole 24 hours, 146/91 mmHg for day time and 127/79 mmHg for night time.<sup>(8)</sup> Day time average blood pressure values at or below 135/80 mmHg correlate with normal left ventricular muscle mass<sup>(9)</sup> and can, for the purpose of evaluating the prospective living donor, be considered normal.

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 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.

## 10.2 THE HYPERTENSIVE PROSPECTIVE DONOR

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, in a potential donor with well-controlled hypertension and no evidence of end organ damage, many units would be prepared to undertake kidney donation. Others would be reluctant to proceed on the basis that uninephrectomy may worsen the problem.

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  $\leq 83$  mmHg.<sup>(11, 12)</sup> 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.<sup>(4)</sup>

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 or on the incidence of complications from hypertension. Because individuals with hypertension and those on anti-hypertensive therapy are commonly excluded as kidney donors, there is relatively little information available. Torres *et al* carried out a longitudinal study of blood pressure measurement in living kidney donors followed up for at least 10 years.<sup>(13)</sup> Ten of 66 kidney donors who were normotensive at the time of donation subsequently became hypertensive 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 the condition and suggested that individuals with borderline or treated hypertension should be advised not to donate. 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.<sup>(14)</sup>

#### 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 (diastolic  $\leq$  83 mmHg). They should be warned of the possibility that nephrectomy may increase their blood pressure.

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## 11.0 Diabetes mellitus

The presence of diabetes mellitus (Type 1 and Type 2) in a prospective donor is an absolute contraindication to kidney donation. Individuals with diabetes may have either overt or subclinical renal impairment. In the evolution of diabetic nephropathy, hyperfiltration precedes the development of microalbuminuria, which heralds the onset of overt nephropathy.<sup>(1, 2)</sup> Unilateral nephrectomy may, in addition to reducing renal reserve, further accelerate the development of nephropathy in the residual kidney. Unfortunately, there is little clinical information on whether or not uninephrectomy increases the risk of developing nephropathy and if so by how much.<sup>(3, 4)</sup> Diabetics, especially if poorly controlled, are also at increased risk from complications during general anaesthesia and surgery.<sup>(5)</sup>

### 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.<sup>(6)</sup> A fasting venous plasma glucose of > 7.0 mmol/l indicates diabetes mellitus and donation should not proceed.<sup>(6)</sup> 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.<sup>(7)</sup>

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  $\geq 11.1$  mmol/l indicates diabetes.<sup>(6)</sup> A value of  $\geq 7.8$  mmol/l indicates impaired glucose tolerance. Caucasians in this latter category have a 10% 5 year risk of diabetes.<sup>(7)</sup> The risk is higher for certain ethnic groups, notably individuals from Southern Asia and the Caribbean.<sup>(8)</sup> Testing for glycosuria and measurement of random glucose levels has low sensitivity in the diagnosis of diabetes.<sup>(9)</sup>

After exclusion of pre-existing diabetes, the clinical risk factors for diabetes and diabetic nephropathy should be evaluated and discussed with the potential donor.<sup>(3, 4)</sup>

### 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.<sup>(10)</sup> The incidence of Type 1 diabetes in adults is less than 1 in 10,000.<sup>(10)</sup> 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.<sup>(11)</sup> However, because Type 1 diabetes is relatively uncommon and most cases have presented before the age at which live 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.

### 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 unrecognised.<sup>(12)</sup> The crude prevalence of undiagnosed disease in the Caucasian population is 2.3%.<sup>(13)</sup> 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%).<sup>(14)</sup> The combination of family history and obesity (BMI  $\geq$  30) places an individual at very high risk of diabetes in later life.<sup>(15)</sup>

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 life time risk of Type 2 diabetes is very high<sup>(16, 17)</sup> 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.<sup>(18)</sup> However, there is a 50% cumulative incidence of proteinuria after Type 2 diabetes mellitus has been present for 20 years<sup>(19)</sup> which may reasonably become an issue for kidney donors who have an above average life expectancy and may expect to live to their 80s.<sup>(20)</sup> 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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### 12.1 PROTEINURIA

Urine protein excretion should be estimated in 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 semiquantitative and not by itself sufficient. A correctly performed 24 hour 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.<sup>(1, 2)</sup> 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.<sup>(3)</sup>

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 24 hour protein excretion does not usually exceed 1g. The pathogenesis of the condition is unclear but in virtually all cases it is benign<sup>(4-6)</sup> and is not usually considered a contraindication to kidney donation. 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.<sup>(7)</sup> Transient proteinuria sometimes occurs in response to exercise or fever.

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

### 12.2 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.<sup>(2, 8)</sup> 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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Standard reagent strips often produce false positive but rarely produce false negative results.<sup>(1, 2)</sup> If routine screening of the urine with reagent strips is negative for blood, microscopic haematuria can be reliably excluded. If the initial reagent strip test is positive for blood the test should be repeated on subsequent visits. If testing is negative on three occasions, further concern is unnecessary. Sporadic haematuria is relatively common. Causes of benign transient haematuria such as exercise, trauma or fever will be discovered from the routine history.

Examination of the urine sediment may be helpful in confirming the presence of red cells, and identifying the presence of cellular casts that indicate glomerular bleeding.<sup>(3)</sup> However, it is essential that fresh urine is examined. Red cells lyse in stored urine and negative results must be interpreted with caution.

In the context of the potential living kidney donor with persistent microscopic haematuria, it is necessary to proceed to a full work up with urine culture, microscopy and cytology, cystoscopy and renal imaging. If no urological cause for haematuria is found a renal biopsy should be performed. Common urological causes of microscopic haematuria are infection, nephrolithiasis and urothelial carcinoma. Glomerular causes include IgA nephropathy, thin basement membrane nephropathy and hereditary nephritis.<sup>(4-9)</sup>

*Best Practice: Isolated microscopic haematuria is not a contraindication to living donation. However, persistent microscopic haematuria requires full investigation to identify an underlying cause. Kidney donation should only proceed if urological and nephrological assessment is normal.*

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## 14.0 Nephrolithiasis

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Nephrolithiasis is a relative contraindication to kidney donation because the donor is at risk of further stone disease. Inadvertent transplantation of a kidney containing a stone may also harm the recipient although this is uncommon.<sup>(1)</sup> The prevalence of nephrolithiasis in the UK is around 3-5% and the incidence of symptomatic stone disease is about 0.5% per year.<sup>(2)</sup> Patients who have passed a stone are significantly more likely to pass additional stones<sup>(2)</sup> and up to 50% of patients with a calcium stone will pass a further stone within 5 years.<sup>(3, 4)</sup>

Biochemical assessment should be undertaken in prospective donors with a history of urinary stones or if there are risk factors for stone disease and specialist advice should be obtained. The composition of a stone may help identify a predisposing cause.<sup>(5, 6, 7)</sup> Calcium oxalate stones account for around 80% of all stones and many cases are associated with varying degrees of idiopathic hypercalciuria.<sup>(8, 9, 10)</sup> Struvite stones are associated with infection by urea splitting organisms. They represent around 15% of all stones<sup>(8, 9)</sup> and are usually considered an absolute contraindication to donation. Cystine, uric acid and calcium phosphate stones<sup>(8, 9)</sup> account for 2-5% of stones and usually preclude kidney donation.

When a potential donor 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.<sup>(11)</sup>

The metabolic risk factors for stone formation include hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitraturia. Investigations should include plasma calcium and uric acid levels, together with 24 hour collection for estimation of calcium, oxalate, uric acid, citrate and cystine.<sup>(12, 13)</sup>

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.<sup>(14)</sup> 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 donor kidney 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 which previously passed the stone for transplantation. The donor should be advised of the importance of ensuring a good fluid intake to reduce the risk of further stones.

*Best Practice: A history of nephrolithiasis is not an absolute contraindication to donation if the disease has been inactive for ten years and there are no predisposing metabolic conditions. 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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## 15.0 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 excluding the disease in the genetically related potential donor.<sup>(1)</sup>

Knowledge of the clinical features of the disease, age of onset and pattern of inheritance is important. 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

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. Diagnosis of ADPKD is based on the following radiological criteria:

- At least two cysts unilaterally or bilateral single cysts in individuals aged less than 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 over the age of 60 years.<sup>(4)</sup>

A negative renal ultrasound beyond the age of 30 years virtually excludes ADPKD.<sup>(1-4)</sup>

Between the ages of 20-30 years a negative ultrasound should be followed by a CT scan. Genetic linkage studies may be useful if there are two or more affected family members.

Alport's syndrome is most commonly inherited as an X linked disorder of type IV collagen.<sup>(5)</sup> The average age of ESRF in males is 21 years. The clinical course in female carriers is extremely variable.<sup>(6)</sup> 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 nephrologists and clinical geneticists.

Vesico-ureteric reflux 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 relatives being considered as donors. A history of enuresis or urinary infections as a child is common in affected individuals. Isotope renography is a sensitive way of detecting renal scars and can be used to look for indirect evidence of reflux in potential donors.

*Best Practice: When the cause of renal failure in the potential recipient is due to an inherited condition (other than Adult Polycystic Kidney Disease), consideration of a relative as a potential donor should be undertaken in conjunction with a clinical geneticist.*

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## 16.0 Donor malignancy

The accidental transmission of malignant disease from donor (cadaveric or living) to recipient by kidney transplantation is well described.<sup>(1)</sup> 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.<sup>(2)</sup> 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 cadaveric 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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Identification of current or previous infection in the prospective kidney donor is an important aspect of donor evaluation. The presence of active infection usually precludes donation. Apart from the implications of infection for the health of the prospective donor, a number of infections may be transmitted by organ transplantation. Those that are of established clinical significance are listed in Tables 17.1 and 17.2.

**Table 17.1**  
Transmissible viral infections of established clinical significance

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Human immunodeficiency virus (HIV-1 and HIV-2)
Human T lymphotropic 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)

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**Table 17.2**  
Transmissible bacterial, fungal and parasitic infections of established clinical significance

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<b>Bacterial</b>
Bacterial meningitis
<i>Mycobacterium tuberculosis</i> (MTB)
Atypical mycobacterial infections
Syphilis*
<b>Fungal and parasitic</b>
Malaria
Toxoplasmosis
Schistosomiasis

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\*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.

## 17.1 EVALUATION OF THE PROSPECTIVE DONOR

A detailed clinical history is important and should include a psychosocial history to define at-risk behaviour, (see Table 7.3 in Section 7.0). 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 7.5 in Section 7.0 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. 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 17.3. 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 to counsel 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.

## 17.2 VIRAL INFECTIONS IN THE PROSPECTIVE DONOR

### HIV

The presence of HIV or human T lymphotropic 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. the Caribbean. 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.<sup>(1, 2)</sup> The risk of HCV transmission from an HCV positive donor approaches 100%.<sup>(3)</sup> 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 checked. HBV DNA testing should be performed in prospective donors from HBV endemic areas, those with possible mutant HBV and those with abnormal liver tests or a past history of liver disease of unknown aetiology.

There are occasional reports of kidneys transplanted from HB surface antigen-negative, HB core antibody-positive cadaver donors with a low risk of HBV seroconversion and no excess risk of graft failure or short-term morbidity.<sup>(4, 5)</sup> For recipients of a kidney from an HBV positive donor, a combination of vaccination, HBV immunoglobulin and anti-viral drugs could be considered.

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

### Cytomegalovirus

Cytomegalovirus (CMV) infection is the most commonly encountered clinically significant viral infection after kidney transplantation<sup>(6)</sup> 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.

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 (as suggested in Table 17.4) or close monitoring and pre-emptive therapy should be offered. It is not currently possible to recommend the best of several effective regimes.<sup>(7, 8, 9)</sup> When transplantation of a kidney from a CMV-seropositive donor to a CMV-seronegative recipient is undertaken, 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 screened sequentially after transplantation or given CMV prophylaxis/treatment according to the stated policy of the transplant unit.*

### Epstein-Barr virus

Primary Epstein-Barr virus (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 anti-lymphocyte antibody immunosuppressive therapy. Consideration should be given in this situation to the prophylactic use of antiviral agents (Acyclovir or Ganciclovir) in order to minimise the viral load after transplantation. This strategy may protect renal transplant recipients from PTLD<sup>(10)</sup> but is not of benefit in paediatric liver transplant recipients<sup>(11)</sup>. 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.

### Varicella-zoster virus

It is important to know whether the potential recipient is Varicella-zoster virus (VZV)-seropositive or not as a primary VZV infection may be rapidly fatal in an immunocompromised host.<sup>(12, 13)</sup>

### Human Herpesvirus 8

Human Herpesvirus 8 (HHV8) may be transmitted by organ transplantation and is associated with an increased risk of Kaposi's sarcoma.<sup>(14)</sup>

### 17.3. BACTERIAL INFECTIONS IN THE PROSPECTIVE DONOR

The main risk of transmissible bacterial infection is from *Mycobacterium tuberculosis* (and in the future increasingly of 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 17.5).

### 17.4 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.<sup>(12)</sup> 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 prion related diseases. Table 17.5 summarises the use of prophylactic antimicrobial agents for different types of donor infection.

**Table 17.3**  
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	*Malaria
*Trypanosoma cruzi	*Trypanosoma cruzi

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

**Table 17.4**  
**CMV prophylaxis**

Donor/recipient serological status	Immunosuppressive regime	Recommendation
Donor negative, recipient negative	Any	None
Donor positive, recipient negative	Conventional	Prophylaxis
Donor positive, recipient negative	Antibody therapy	Prophylaxis
Donor positive, recipient positive	Conventional	Local practice
Donor positive, recipient positive	Antibody therapy	Prophylaxis

Modified from Jassal, *et al* 1998<sup>(7)</sup>

**Table 17.5**  
**Use of prophylactic antimicrobial agents**

1. HBV positive donor	Vaccinate recipient HBV immunoglobulin
2. CMV (donor positive, recipient negative)	Prophylactic antiviral drugs indicated
3. EBV (donor positive, recipient negative)	Consider prophylactic Acyclovir or Gancyclovir
4. Toxoplasmosis	Sulphonamide <i>or</i> Clindamycin <i>or</i> Clarithromycin <i>or</i> Azithromycin <i>or</i> Pyrimethamine
5. Mycobacterial infections	Prophylactic Isoniazid
6. Bacteria	Low virulence: ≤ 7 days of appropriate antibiotic High virulence: ≥ 14 days of appropriate antibiotic

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Living donor renal transplantation requires support from a high quality tissue typing laboratory. Good liaison between the tissue typing laboratory and the clinical transplant team is important and donor/recipient matching and crossmatching policies should be jointly established. It is valuable for both parties to be involved in pre-transplant discussions concerning the selection of potential donors and in post-transplant case conferences. Close collaboration between transplant clinicians and the tissue-typing laboratory ensures the provision of clinically appropriate tests while avoiding unnecessary waste of human and financial resources through inappropriate histocompatibility testing.

### 18.1 MATCHING FOR HLA SPECIFICITIES

HLA typing of donors and recipients should be performed using a (PCR-SSP) polymerase chain reaction – single strand polymorphism technique. The choice of an HLA matched donor within a family is restricted by the absolute need for ABO blood group compatibility. Rhesus blood groups can be safely ignored in donor selection.

The degree of compatibility for HLA between a donor and recipient is commonly expressed as the degree of HLA mismatching. A convenient three digit score is used as shorthand to indicate the degree of HLA-A, -B and -DR mismatch between a donor and recipient. A zero HLA mismatch is designated “000” and a complete mismatch is

designated “222”. A haplotype matched sibling donor will usually be a “111” mismatch but may share additional HLA specificities due to chance compatibility of common HLA types.

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 only one HLA haplotype but may fortuitously share more HLA specificities.

*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 foreign HLA.*

The possibility of matching recipient HLA with that of distant genetic relatives or unrelated donors such as spouse or friends is little different to the chance of matching in cadaver donor kidneys. It should be remembered that when a completely mismatched kidney transplant fails because of rejection the recipient may become highly sensitised,<sup>(1)</sup> restricting options for repeat transplantation, at least in the short term.

Kidney transplantation from an adult offspring to mother and from a father to the mother of his children has to be approached with care due to the

possibility of pregnancy-related, donor HLA-specific sensitisation. Such transplants are often excluded because of a positive crossmatch. There is limited information on the outcome of those transplants undertaken when the crossmatch is negative. However, the international databases (Collaborative Transplant Study [CTS] and United Network for Organ Sharing [UNOS]) suggest that the outcome is similar to that for other non HLA identical living donor transplants.<sup>(2,3)</sup>

*Best Practice: HLA typing of potential donors should not be performed until ABO compatibility with the recipient is established. This saves significant costs. When there is an option of selecting between living donors then HLA matching should be considered as a benefit.*

A widely cited publication of the experience of living unrelated spousal donor kidney transplantation in North America<sup>(3)</sup> established that graft survival rates for such transplants is equivalent to that of HLA mismatched living related donor kidney transplants at 82% at three years of follow-up. This equates with the smaller UK experience (see Table 21.1 in Section 21) but exceeds the North American experience for matched cadaver donor kidney transplants of 70% at three years. The same authors reported no benefit from HLA-DR matching in living unrelated donor kidney transplants except that the predicted half-life was greater in

zero HLA-DR mismatched cases.<sup>(3)</sup> In contrast, the CTS reported on HLA mismatching in 2281 unrelated living donor kidney transplants and found a significant reduction in graft survival when transplants were mismatched at HLA-A, -B and -DR.<sup>(2)</sup> However, graft survival is at least equivalent to that of cadaveric donor transplantation.

## 18.2 RECIPIENT ANTIBODY SCREENING

Recipients should be screened for the presence of clinically relevant, potentially harmful antibodies in a manner equivalent to that for patients awaiting cadaver donor kidney transplantation. Some centres ensure this by entering all potential living donor kidney recipients on the cadaver donor waiting list in the “suspended” category. Serum samples should be obtained for antibody screening at least twice each year and following all potential sensitising events. A comprehensive cytotoxicity screening technique is the minimum requirement and an additional flow cytometric-screening assay is recommended. Commercially available ELISA screening techniques are being used increasingly and offer improved assay standardisation, increased sensitivity and assignment of specific sensitisation.<sup>(4)</sup> The use of agents such as DTT to reduce IgM antibodies in patient serum samples aids the identification of clinically irrelevant IgM autoreactive antibodies, although the presence of potentially graft damaging IgM alloantibodies must be considered.

An accurate report of the patient’s sensitisation status can only be made after

careful interpretation of test results. There is an important need for the histocompatibility laboratory to receive data on possible sensitising events such as failed transplants, pregnancies, past blood transfusions and immunosuppression with antibody therapy to facilitate identification of unacceptable HLA specificities and false positive antibody screening results.

*Summary point: Screening of potential living donor kidney transplant recipients for clinically relevant antibodies is probably the most important contribution of the histocompatibility laboratory towards ensuring optimal graft survival.*

### 18.3 THE DONOR/RECIPIENT CROSSMATCH TEST

The presence of pre-formed antibodies directed against HLA antigens expressed by the prospective donor may result in hyperacute or accelerated acute rejection if transplantation is undertaken. A positive crossmatch test therefore precludes living donor kidney transplantation unless the antibody responsible has been shown to be clinically irrelevant. When the antibody responsible has specificity for HLA, transplantation is contraindicated, irrespective of the nature of the target cells used (e.g. T or B cells), the antibody class (IgG or IgM) and the timing of the serum sample.

The crossmatch test should be performed at an early stage in the evaluation of a prospective donor so that if it is positive further unnecessary evaluation can be avoided. A positive crossmatch must

always be interpreted in the light of full antibody screening results, clinical events and sensitisation history. It is essential to identify false positive crossmatches due to clinically irrelevant antibodies and to determine the clinically relevant sensitivity of the crossmatch and antibody screening techniques used. Kidney transplant units should define their own criteria for a “negative” and “positive” crossmatch. A false positive crossmatch result may result in a suitable donor being excluded and a false negative crossmatch may result in early graft loss if transplantation proceeds.

A pre-transplant serum sample should be collected within one week of the planned date for transplantation and tested in a sensitive crossmatch to confirm that it is safe for transplantation to proceed. Blood transfusion after the final crossmatch should be avoided whenever possible but if it is essential then transplantation should be deferred.

The technique used for the crossmatch test should be sensitive and clinically relevant. The use of a flow cytometric technique is recommended particularly for sensitised patients and re-transplantation. The conventional cytotoxicity crossmatch is not sufficiently sensitive to detect all clinically relevant antibodies. Moreover, clinically irrelevant antibodies such as IgM autoreactive antibodies may give a false positive result. Cytotoxicity crossmatching using a sensitive assay with prolonged incubations and T and B lymphocyte target cells isolated from donor peripheral blood with immunomagnetic beads may be useful for

excluding potential donors to whom the recipient is sensitised. Once a transplant date has been arranged, however, a flow cytometric crossmatch should be performed. If a sensitive antibody screening technique, such as ELISA, is 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 the timing of samples with respect to the planned date for transplantation and to the specificity of any antibody identified.

Careful consideration must be given to the sensitisation status and crossmatch results for proposed offspring to mother or husband to wife donation where donor specific sensitisation through previous pregnancy may have occurred. Some centres perform donor specific blood transfusions in these instances in an attempt to reveal possible sensitisation by provoking an antibody response. If this approach is used it should be performed in close collaboration with a Consultant Haematologist.

*Best Practice: Kidney transplant units should carefully define their interpretation of what constitutes a positive and negative crossmatch. This should be based on a thorough review of their own experience and that in the published literature. A pre-transplant serum sample collected within one week of the planned date for transplantation should be tested in a sensitive crossmatch and if the crossmatch test is positive transplantation should not be performed unless the antibody has been shown to be clinically irrelevant.*

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## 19.1 GENERAL CONSIDERATIONS

The consent of the donor to undergo nephrectomy is made on the understanding that it will be performed by an experienced and competent surgeon and that all possible steps will be taken to reduce the incidence of peri-operative complications.

Responsibility for the donor lies ultimately with the surgeon performing the donor nephrectomy. 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 donor kidney is removed from the donor only after it has been confirmed that there are no unforeseen problems with the recipient that prevent implantation. The alternative arrangement of sequential donor recipient operations is less desirable.

Living donor transplantation from an adult donor into a child recipient demands special consideration. 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 visit each other soon after the transplant operation. 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.

## 19.2 PROPHYLAXIS OF VENOUS THROMBOEMBOLISM

It is particularly important to question potential donors about symptoms suggestive of a previous deep venous thrombosis (DVT).

In 1992 Najarian *et al*<sup>(1)</sup> documented 17 donor deaths in the USA, Canada and Europe. Seven of the deaths reported were attributed to pulmonary embolus (PE). 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.<sup>(2)</sup>

- Increasing age
- Obesity
- Immobility (bed rest over 4 days)
- High dose oestrogens (50µg oestrogen or more per day)
- Previous DVT or PE
- Thrombophilia
- Paralysis of lower limb(s).

Hospitalised patients with previous DVT or PE and patients with lower limb paralysis or thrombophilia are at “high risk” of thromboembolism. The reported incidence of proximal vein thrombosis in “high risk” patients is 10-30% and the incidence of fatal pulmonary embolism is 1-10%.<sup>(3)</sup> The view of the working party is that potential kidney donors who fall into the “high risk” category should only be considered further for organ donation under exceptional circumstances.

Females on oestrogen treatment should discontinue treatment before undergoing donor nephrectomy.

Early mobilisation should be encouraged after living donor nephrectomy. Patients over the age of 39 years 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.<sup>(3)</sup> Patients under the age of 40 years undergoing major surgery, in the absence of additional risk factors, are classified as “low risk”. Guidelines recommend that they should be encouraged to mobilise early but do not merit the risks and costs of routine specific prophylaxis with antithrombotic drugs or mechanical devices.

All kidney donors over the age of 39 years therefore fall into the “medium risk” category and should be given specific prophylaxis against venous thromboembolism. Healthy kidney donors

under the age of 40 years, with no additional risk factors for venous thromboembolism, could be categorised as “low risk”. However, it cannot be assumed that such patients will always be mobile within 4 days and the working party recommends strongly that all kidney donors, irrespective of age, should be regarded as “medium risk” and given specific prophylaxis. 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 (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.<sup>(4)</sup> Prophylaxis should continue for at least 5 days (the minimum duration in clinical trials) or until discharge from hospital if this is earlier.

Thrombocytopenia 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<sup>(3)</sup> and are not recommended as alternatives to heparin prophylaxis in kidney donors.

Mechanical methods for prophylaxis include graduated elastic compression stockings<sup>(5)</sup> and intermittent pneumatic compression 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. 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.

*Best Practice: High risk of venous thromboembolism is a relative contraindication to a living renal donation. All kidney donors should receive prophylaxis comprising low dose or low molecular weight heparin (starting prior to surgery and continued for at least 5 days or until discharge), supplemented with mechanical methods such as graduated elastic compression stockings and/or intermittent pneumatic compression devices.*

### 19.3 DONOR NEPHRECTOMY

A number of different surgical approaches have been used for living donor nephrectomy and no particular approach has been shown to be superior. Donor nephrectomy is most commonly undertaken by a retroperitoneal approach via a loin incision, with or without resection of a rib.<sup>(6)</sup> The extensive loin incision is a potential source of severe short-term pain and may also give rise to long term wound discomfort. For the donor, the prospect of wound pain is one of the most worrying aspects of the operation.

It is important to ensure adequate analgesia after surgery. The use of local anaesthetic wound infiltration, patient controlled analgesia with intravenous morphine and epidural analgesia have limited but not completely removed this problem. A small but significant number of patients develop prolonged wound discomfort, which may require referral to a pain clinic.

The anterior extraperitoneal approach is sometimes preferred and provides good exposure of the kidney vasculature.<sup>(7, 8)</sup>

Some transplant surgeons prefer to perform the nephrectomy using a transperitoneal approach through a midline or transverse incision when performing donor nephrectomy and maintain that it is associated with less wound pain than the loin approach.<sup>(7)</sup> A potential problem is the development of intestinal obstruction as a result of peritoneal adhesions.<sup>(9)</sup>

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

#### 19.4 LAPAROSCOPIC DONOR NEPHRECTOMY

Recently, donor nephrectomy has been performed using minimally invasive surgery. The first laparoscopic living donor nephrectomy was carried out in 1995 at the Johns Hopkins Medical Centre and since then many centres in the USA and elsewhere, including at least two in the UK, have undertaken laparoscopic living donor nephrectomy. Advocates of laparoscopic nephrectomy (or laparoscopic assisted nephrectomy) argue that it substantially reduces the wound-related problems associated with open nephrectomy.<sup>(11-14)</sup> There have not been any controlled clinical trials of laparoscopic versus open living donor nephrectomy. However, blood loss, requirement for post-operative analgesia, length of hospital stay and time until return to normal activity are all lower in patients undergoing laparoscopic nephrectomy than in historical controls undergoing open nephrectomy.<sup>(11-14)</sup> During laparoscopic nephrectomy, warm ischaemia times of 3-5 minutes are reported, raising concern that ischaemic injury may result. Although data following laparoscopic living donor nephrectomy is still limited, immediate function rate and graft survival appear broadly comparable to that reported for open nephrectomy. Laparoscopic living donor nephrectomy requires expertise in advanced laparoscopic techniques and should only be undertaken by surgeons with appropriate training in the technique. This requirement may limit the availability of laparoscopic living donor nephrectomy in the UK, at least for the time being.

#### 19.5 DONOR BLOOD TRANSFUSION

Living donors may occasionally require blood transfusion during the peri-operative period. If available, prospective donors should be offered the opportunity to have autologous blood transfusion.

#### 19.6 DONOR SPECIFIC TRANSFUSION

Donor specific blood transfusion before living donor transplantation is used by some centres on the basis that it may promote subsequent graft survival.<sup>(15)</sup> However, it may also result in the development of cytotoxic antibodies in the prospective recipient and thereby preclude transplantation. It is not widely practised and if undertaken must be done so with close involvement of both a haematologist and the histocompatibility laboratory.

#### 19.7 PRE-TRANSPLANT IMMUNOSUPPRESSION

Some transplant centres start the recipient on immunosuppressive therapy several days before living donor transplantation. This approach allows optimisation of drug levels before surgery but it is not known whether this improves patient management or outcome.

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## 20.0 Donor follow-up

### 20.1 ARRANGEMENTS FOR FOLLOW-UP

Early follow-up of the donor is essential to ensure that they have made a satisfactory recovery from their operation. In the event of an unsuccessful transplant it is important to provide counselling facilities for the donor. Current practice with respect to long term follow-up varies widely between centres. In a recent survey 28 UK centres reported their policy on long-term follow-up of living donors.<sup>(1)</sup> Eighteen 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.<sup>(1)</sup> In the US, only 13 % of UNOS approved centres recommend indefinite donor follow-up.<sup>(2)</sup>

There are no good data on which to base recommendations for the nature and duration of follow-up of kidney donors. It seems reasonable, however, to recommend that donors are evaluated at least annually to measure their blood pressure, check their renal function and examine their urine for proteinuria. Life-long follow-up is recommended. In donors at increased risk, follow-up should be more frequent. The transplant centre, nephrology unit or the patient's GP may undertake follow-up. Donors should be advised to take care if participating in activities that might involve trauma to the remaining kidney.

A UK register of kidney donors is currently being set up under the auspices of UKTSSA. When the live donor register has been established, Units in the UK undertaking living donor kidney

transplantation should submit prospective information on all living donor kidney transplants.

### 20.2 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.<sup>(3)</sup> Another study of 23 viable births in 14 kidney donors reported no significant problem.<sup>(4)</sup>

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 urine culture and blood pressure should be undertaken.

*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 live donor register. Life long follow-up is recommended.*

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## 21.0 Recipient outcome after living donor kidney transplantation

Clinical audit should be an integral part of the work of the transplant unit.

Patient survival, morbidity and transplant outcome depend critically upon a number of casemix factors such as the age and comorbidity of the population transplanted. These in turn depend upon the criteria for selecting patients as potential transplant recipients, and more remotely, on the criteria for acceptance on to dialysis. All transplanted kidneys retrieved from living donors should be expected to function immediately.

### 21.1 MEASURING OUTCOME

It has been possible to audit the outcome of kidney transplantation in the UK because a national transplant database and comprehensive follow-up has existed for more than 25 years.<sup>(1)</sup> Factors used as measures of transplant outcome include:

- Survival of the transplanted kidney
- Survival of the recipient
- Incidence and timing of acute rejection episodes
- Incidence of tumours
- Incidence of chronic transplant nephropathy
- Quality of life measurements.

### Recipient survival after living donor renal transplantation

The patient survival of 674 UK living donor kidney transplants (1989-1997) is 97% at one year and 91% at five years when the donor is a parent or sibling but the five year figure falls to 72% when the relationship was not recorded.

### Graft survival after living donor renal transplantation.

Graft survival following living donor kidney transplantation in the UK exceeds 90% at one year and 80% at five years for first grafts and 77% at 5 years for repeat transplants.

The relationship between donor and recipient for 1163 living donor kidney transplants performed in the UK between 1989 and 1997 is shown in Table 21.1 (data supplied by UKTSSA).

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

*Standard: Graft survival after living donor kidney transplantation should be at least 90% at one year and 80% at five years*

**Table 21.1. Relationship between donor and recipient and graft survival in living donor kidney transplants performed in the UK, 1989 to 1997**

Relationship of living kidney donor to recipient	Percent of 1163 living donor kidney transplants in the UK	Five year graft survival (percent)
Parent	47.2	82.2
Sibling	42.6	89.1
Offspring	0.4	
Other relative	6.4	72.5
Unrelated (87.8% of which were spouse/partner)	3.4	

The UK data shows that a close genetic relationship gives high survival rates; many of the sibling donor transplants will have a low degree of HLA mismatching (see Table 21.3).

The UK data on outcome of living donor kidney transplants, irrespective of donor/recipient relationship, in 1989 to 1997 in

relation to HLA mismatching is shown in Table 21.2.

The UK outcome data for 1990 to 1997 combining relationship and HLA mismatching is shown in Table 21.3. The number of cases of genetically unrelated donor transplants (n=24) is too small for meaningful outcome analysis.

**Table 21.2. HLA mismatch and graft survival after living donor transplantation in the UK**

HLA-A, -B, -DR mismatches	Number of transplants	Percent graft survival:	
		(one year)	(five years)
Zero	161	92	90
One	90	92	87
Two	182	90	85
Three	217	89.5	79

**Table 21.3. Donor/recipient relationship and graft survival after living donor transplantation in the UK**

Relationship of donor to recipient	Degree of HLA mismatch	Number of transplants	Percent graft survival:	
			(one year)	(five years)
Sibling donor	000 and "favourable" match	148	93.8	93.8
	Other mismatches	130	90.3	76.5
Parent donor	000 mismatch	30	93.3	93.3
	Other "favourable" match	78	98.7	83.6
	Other mismatches	246	91.1	78.1

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Living donor transplantation for high risk recipients, i.e. recipients who are at high risk of death with a functioning transplant or graft failure, requires special consideration. It is important that the donor and recipient are given a realistic estimate of a successful outcome after transplantation. High risk patients include those with severe cardiovascular disease, pulmonary disease, diabetes mellitus and obesity as well as those who are unlikely to comply fully with their immunosuppressive therapy.<sup>(1,2,3)</sup> Recipients for living donor transplantation should usually fulfil similar criteria to those required for cadaveric transplantation. Occasionally, there may be high risk cases where living donor transplantation is the most appropriate form of treatment. In general, however, living donor transplantation should only be undertaken where there is a good chance of a successful outcome for the recipient in terms of improved quality of life for a reasonable length of time.

*Best Practice: Recipients of living donor transplants should fulfil the same criteria with regard to co-morbid conditions as those set prior to listing for cadaveric transplantation. Donor and recipient should be given a realistic estimate of the chance of a successful outcome.*

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## 23.0 Recurrent renal disease

Many of the diseases responsible for chronic renal failure may affect a renal allograft.<sup>(1)</sup> The important issues to consider are:

- The likelihood that a particular disease will affect a transplant
- 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

### 23.1 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 cadaveric renal transplantation be undertaken or that pre-emptive liver transplantation be performed.<sup>(2-4)</sup> Some North American groups advocate early living donor kidney transplantation.<sup>(2,5)</sup> 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.

### 23.2 IgA NEPHROPATHY

IgA nephropathy commonly recurs following renal transplantation. The recurrence rate, based on graft biopsy, has been reported to be around 80% in living related transplantation<sup>(6)</sup> and 60% in a series of cadaveric grafts.<sup>(7)</sup>

However, considerable experience, especially in recipients of cadaveric grafts, shows that graft survival in patients with IgA nephropathy compares favourably with that in patients with other causes of renal failure. Living donor transplantation is not, therefore, contraindicated.

The recurrence rate in active Henoch Schönlein purpura is reported to be as high as 80% and some authorities have recommended waiting one year after the end of the purpuric eruption before considering renal transplantation.<sup>(8)</sup>

### 23.3 MEMBRANOUS GLOMERULONEPHRITIS

There have been reports of membranous glomerulonephritis recurring within the first few months following living related transplantation.<sup>(9-11)</sup> Because the reported experience is small, it is difficult to give more than an estimate of the risk. Where the course of the original glomerulonephritis was fulminant with the rapid development of renal failure it would be prudent to avoid living donor kidney transplantation. If the course of the original disease extended over many years, living donor kidney transplantation may be a reasonable option.

### 23.4 DIABETES MELLITUS

Biopsies of kidney allografts taken more than two years after transplantation in diabetic recipients show glomerular changes consistent with diabetic nephropathy.<sup>(12)</sup> 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.<sup>(13)</sup>

### 23.5 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.

### 23.6 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.<sup>(14)</sup> 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.

### 23.7 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,<sup>(15-17)</sup> and the risk of recurrence appears to be higher, the younger the child at the onset of the disease.<sup>(18, 19)</sup> Rapid progression of FSGS with fulminant ESRF in children also correlates well with recurrent disease.<sup>(20)</sup> Living donor kidney transplantation in children with FSGS therefore carries a high risk of recurrent disease and premature graft failure.

It has been reported that if FSGS does not occur in a primary graft then subsequent renal transplants will remain free of the disease.<sup>(21)</sup> Conversely, when three individuals lost their first graft within 13 months from recurrent FSGS their 7 subsequent grafts were all lost within 38 months; six of those grafts were lost within five months. In eight adult recipients of living donor kidneys in Japan, four promptly lost their grafts to recurrent FSGS. Three others were treated with plasma exchange although the role of this treatment in preventing recurrent FSGS is unproven.<sup>(22)</sup> In the future, identification of an "FSGS factor" and its removal may allow a more informed decision to be made about the risk of recurrent disease.<sup>(23)</sup> Two siblings who were living donors for recipients with familial FSGS subsequently developed ESRF failure, one with biopsy-proven FSGS. Both individuals had a normal routine evaluation before donation.<sup>(34)</sup>

This anecdote argues for great caution in utilising siblings as donors for recipients with FSGS.

*Best Practice: Living donor kidney transplantation should be avoided for children with FSGS and for adults with fulminant FSGS. Re-transplantation from a living donor is reasonable if a previous graft showed prolonged function or was free of FSGS.*

### 23.8 ALPORT'S, CRESCENTIC GLOMERULONEPHRITIS, VASCULITIS

Recurrent anti-glomerular basement membrane (GBM) disease in allografts is rare.<sup>(25)</sup> *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. 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.

### 23.9 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.<sup>(26)</sup> 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.<sup>(27)</sup> 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.<sup>(28)</sup> Inherited HUS, although rare, frequently recurs after transplantation and it is important, therefore, to explore the family history in HUS.<sup>(29, 30)</sup> If, in the future, genetic markers for inherited HUS become available these will aid counselling.<sup>(31)</sup> In idiopathic HUS when there is more often an indolent presentation and collapsed ischaemic glomeruli with marked afferent arteriolar intimal hyperplasia<sup>(32)</sup> there is a high chance of recurrence after transplantation (2 out of 5 cases).<sup>(33)</sup> The reported two-year graft survival in this setting is very poor at 35%.<sup>(34)</sup>

*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.*

### 23.10 SYSTEMIC LUPUS ERYTHEMATOSUS

Recurrent lupus nephritis is reported to occur in around 2-4% of patients requiring renal transplantation because of ESRD due to Systemic Lupus Erythematosus (SLE).<sup>(35-39)</sup> Recurrence of nephritis does not always lead to graft failure. In most reported series, kidney allograft survival in recipients with SLE is similar to that observed in non-diabetic recipients with ESRD due to other causes.<sup>(35-39)</sup>

In those series reporting increased graft loss in patients with SLE, early graft loss due to thrombotic events may be a factor. Thrombotic events have recently been shown to be associated with antiphospholipid antibodies and these are found, with increased frequency in SLE.<sup>(40, 41)</sup> In patients with SLE who have raised antiphospholipid antibodies, careful attention should be paid to peri-operative anti-thrombotic prophylaxis. There is no information on whether longer term anticoagulation is beneficial in such patients.

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, such as levels of complement and anti-double stranded DNA antibodies are not reliable predictors of recurrent disease.<sup>(35, 36)</sup>

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

### 23.11 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.<sup>(42)</sup> 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,<sup>(43)</sup> 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<sup>(43)</sup> 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 transplantation is contraindicated in MCGN type 1. Living donation should usually be avoided as the primary graft in MCGN type II but may be considered as a second or subsequent transplant where there has been prolonged survival of a preceding graft.*

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## 24.0 Appendices

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### 24.2 APPENDIX 2 Acknowledgements

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following: Mr Ali Bakran, Dr Eleanor  
Bolton, Dr John Bradley, Dr Peter Doyle  
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Jamieson, Mr Paul Lear, Dr Richard  
Moore, Mr Keith Rigg, Dr Ken Smith, Dr  
Craig Taylor and Dr Nick Wareham.

**ADPKD**

Autosomal dominant adult polycystic kidney disease.

**ASTP**

American Society of Transplant Physicians.

**ATN**

Acute tubular necrosis.

**BMI**

Body mass index.

**BSHI**

British Society for Histocompatibility and Immunogenetics. The professional organisation for Tissue Typing Laboratory scientists.

**BTS**

British Transplantation Society.

**CTA**

Computed tomographic angiography.

**CTS**

Collaborative Transplant Study.

**CMV**

Cytomegalovirus.

**CROSSMATCHING**

Crossmatch between the recipient's serum and donor lymphocytes testing for the presence of antibodies against white cells.

**DTPA**

Diethylenetriamine penta-acetic acid.

**DVT**

Deep venous thrombosis.

**EBV**

Epstein-Barr virus.

**ESRD**

End stage renal disease.

**ESRF**

End stage renal failure.

**FSGS**

Focal segmental glomerulosclerosis.

**GBM**

Glomerular basement membrane

**GFR**

Glomerular filtration rate.

**HBV**

Hepatitis B virus.

**HCV**

Hepatitis C virus.

**HIV**

Human immunodeficiency virus.

**HLA**

Human Leucocyte Antigen. The principle antigens responsible for causing graft rejection.

**HOT ACT**

The Human Organs Transplant Act (1989 and 1983) and accompanying Regulations. The Act prohibits removal and transplantation of organs for any form of profitable gain. It also limits transplantation of organs from living donors unless donor and recipient are established to be closely genetically related or the transplant has been authorised by ULTRA. The Act also established the national organ transplant register.

**HTLV**

Human T lymphotropic virus.

**HUS**

Haemolytic uraemic syndrome.

**IADSA**

Intra-arterial digital subtraction angiography.

**IVU**

Intravenous urogram.

**LRD**

Living related donor.

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**MCGN**

Mesangiocapillary glomerulonephritis.

**MRA**

Magnetic resonance angiography.

**OGTT**

Oral glucose tolerance test.

**PCR-SSP**

Polymerase chain reaction – single strand polymorphism.

**PE**

Pulmonary embolus.

**pmp**

Per million population.

**PTLD**

Post-transplant lymphoproliferative disorder.

**SLE**

Systemic lupus erythematosus.

**UKTSSA**

UK Transplant Support Service Authority.  
A Special Health Authority of the NHS with responsibility for central co-ordination of organ and tissue transplantation in the UK and Ireland.

**ULTRA**

Unrelated Live Transplant Regulatory Authority.

**UNOS**

United Network for Organ Sharing.

**VZV**

Varicella-zoster virus.

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