# Guidelines relating to solid organ transplants from non-heart beating donors

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*When Brigid McNamee's husband John died three people were given the chance of life. Brigid says "as our son Sean grows up he will be able to understand more about his father's gift, something he can be proud of." Reproduced courtesy of UK Transplant*

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# Contents

# Process of writing

In the spring of 2002 the Council of the British Transplantation Society agreed that the Standards Committee (Chair: Dr C G Newstead, Consultant Renal Physician, Leeds Teaching Hospitals Trust) should prepare guidelines relating to this topic. Dr Newstead wrote the first draft in conjunction with Mr S Willis (Transplant Co ordinator, Leeds Teaching Hospitals Trust) drawing extensively on protocols already in existence at Newcastle, Leicester, North and South Thames. Subsequently revisions and original contributions were made by: Mr D Talbot, (Consultant Hepatobiliary and Transplant Surgeon, Freeman Hospital, Newcastle) Mr N V Jamieson (Consultant Transplant Surgeon Addenbrooke's Hospital Cambridge), Miss L Robson Lead Transplant Co-ordinator Freeman Hospital, Newcastle), Dr P Murphy and Dr D Bell (Neuro-ITU Leeds Teaching Hospitals Trust)

A preliminary draft was circulated at the request of The Department of Health to a group of coroners attending a workshop in late November 2002 to solicit comments.

It was subsequently decided after discussion with a number of interested parties including The Council of the BTS that the BTS guidelines would be altered to cover the management of the process of donation after the diagnosis of death. It would in addition cover the areas of direct involvement of the "Transplant Team" both of the donor and evaluation of the patient who has the potential to become a donor. Excluded from this guidance therefore is the important contribution of other hospital staff for example those working in Accident and Emergency, Intensive Care as well as Coroners.

Other authorities that include: The Intensive Care Society, The Association of Anaesthetists, The Academy of Medical Royal Colleges and Faculties in conjunction with the Department of Health are preparing guidance on the management of the patient who has the potential to become a non-heart beating organ donor.

Authors reviewed contributions made by others, in particular those published in the United States [1, 2].

The likelihood of early changes to British legislation covering this area also led to a reassessment of the document. This change of strategy led to significant editing the subsequent draft was again circulated to the above named colleagues for comment.

After revision the draft was posted on the BTS website for two months from July 2004 and the final version has taken into account constructive comments received from a number of contributors.

In the body of the document key points are shown highlighted.

# Introduction

The number of transplants performed in the United Kingdom has remained virtually static over the last ten years. During this interval the number of donors has decreased by approximately 20%.

The causes for the reduction in heart beating cadaveric donors are multifactorial. There has been a laudable decrease both in fatalities from road traffic accidents in the United Kingdom as well as a significant decrease in the number of deaths from intracranial haemorrhage. Changes in neuro-intensive care management may have contributed.

Renal and other solid organs as well as tissue retrieval from non-heart beating donors is not a new concept. Before the introduction of legislation defining brain stem death in the 1970s all cadaveric kidneys were retrieved from non-heart beating donors.

In Maastricht (Netherlands), Japan and parts of the United States of America as well several units in the United Kingdom, in particular; Addenbrooke's Hospital (Cambridge), Guy's and St George's Hospitals (London), Leicester General Hospital, and Freeman Hospital (Newcastle) have longstanding programmes retrieving organs (principally kidneys) from non-heart beating donors.

As well as the important health benefit acquired by the recipient following successful organ transplantation organ donation can provide benefits to the donor family. Organ donation is usually a positive experience for bereaved families and may be the most comforting aspect of an otherwise tragic and sudden event. Non-heart beating donation in the situation where a patient cannot be diagnosed as dead using brainstem criteria offers the family the choice to donate organs which otherwise would not have been available. It also allows healthcare professionals to carry out the wishes of the deceased when that is known.

*Renal and other solid organs as well as tissue retrieval from non-heart beating donors is not a new concept*

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# Categorisation of non-heart beating donors

These donors can be divided into categories based principally on work from the Maastricht group. This is important both for the logistics of retrieval and outcome following transplantation.

## Category 1: dead on arrival at hospital

For these individuals to be potential donors the moment of sudden death needs to have been witnessed and the time that it occurred documented as well as pre-admission resuscitation.

## Category 2: unsuccessful resuscitation

These are individuals in whom cardio-pulmonary resusitation is commenced following collapse. These patients are usually in an Accident and Emergency Department, in which the interval of resuscitation and the efficiency of resuscitation has been well documented.

## Category 3: awaiting cardiac arrest

These are a group of patients for whom death is inevitable but they do not fulfil brainstem dead criteria. These patients are cared for in many areas within hospitals but most commonly are identified in Neurosurgical Intensive Care Units, General Intensive Care Units, Coronary Care Units, Accident and Emergency Departments and Medical Wards.

## Category 4: cardiac arrest in a brainstem dead cadaver

This is an individual in whom death has been diagnosed by brainstem criteria who then suffers an unexpected cardiac arrest. On some occasions these cases will be awaiting the arrival of an organ retrieval team.

## Category 5: unexpected cardiac arrest in patient in an ITU/ or critical care unit

This has recently been suggested as an addition to the other four categories [3]

# Donor selection criteria

To streamline the process it is helpful for each retrieval team to adopt selection criteria that are known to ITU and A&E as well as donor transplant co-ordinator staff.

## For renal or renal and liver donors

The arbitrary cut off point for something that changes gradually such as age is not logically defensible and referring staff encouraged to discuss all potential donors with donor transplant co-ordinators.

Guide selection criteria:

1. Age<65 years (renal), age <70 years (liver)
2. Warm ischaemic time less than or equal to 20 minutes for the liver and less than or equal to 40 minutes for the kidneys. This time can be defined as starting when there is hypotension below a systolic BP of 55 mmHg and is measured up to the point of the cold perfusion of the organ.
3. No history of renal impairment.
4. No uncontrolled hypertension or complicated insulin dependent diabetes.
5. No uncontrolled systemic sepsis or malignancy using the same criteria as for potential donors who are declared death after brain stem testing.

The "Guidance on the Microbiological Safety of Human Organs, Tissues and Cells used in Transplantation" issued by the Advisory Committee on the Microbiological Safety of Blood and Tissues for Transplantation August 2000 will be followed [4].

## For lung donors

Guide selection criteria:

Aged < 55 years
$P0_2$ / $Fi0_2$ > 30Kpa
No gross abnormality on chest x-ray in past 24 hours. Unilateral changes do not preclude the retrieval of one lung.
Time for the cardiothoracic retrieval team to be present at the withdrawal of treatment.

Contraindications
Previous chest surgery (presence of a chest drain does not preclude donation).
Asthma requiring systemic steroids.
Smoking history, length of ventilation and positive gram stain of airway secretions are not absolute contra-indications.

The Cardiothoracic retrieval team will bring all the equipment they require and transport to and from the hospital is organised by the Cardiothoracic Recipient Transplant Coordinator. The team consists of 2 surgeons, a scrub nurse and a perfusionist. The team will not require any assistance with the bronchoscopy procedure or the retrieval.

*To streamline the process it is helpful for each retrieval team to adopt selection criteria that are known to Intensive Care Units and Accident and Emergency as well as donor transplant co-ordinator staff.*

# Role of the donor transplant co-ordinator prior to death of the donor

### For category 3 and some category 4 donors

When a Donor transplant co-ordinator attends the Intensive Care Unit it will be to assess the patients suitability for non-heart beating organ donation. The assessment will be initially from medical notes and ITU charts and will involve review of:

- Height, weight, ABO blood group, biochemistry
- Ventilation and Oxygenation
- Haemodynamics, ECG, inotropic requirements, urine output, fluid balance
- Medical History
- Social History
- Arterial blood gases (particularly for potential lung donors)

This information will be discussed with a Consultant in Transplantation for their opinion regarding suitability for organ donation. The potential for tissue donation should be explored with competent authorities.

Although the method of treatment withdrawal is dictated by unit policy, the donor transplant co-ordinator must have knowledge of this prior to the next of kin interview.

If the next of kin agree to consider organ donation a Donor transplant co-ordinator will discuss the following issues:

- What happens when death occurs and the need to go to theatre promptly following the certification of death.
- Or the immediate cold preservation of abdominal organs via in-situ perfusion where this is agreed local practice.
- Or circumstances where treatment withdrawal and certification of death takes place in the operating theatre.
- If the time between treatment withdrawal and death is prolonged a point may be reached when organ donation is not possible.
- Medical and social history including completion of UK Transplant's Donor assessment documentation and General Practitioner Questionnaire.
- A lack of objection for blood sampling for either immediate or later testing for virology and other infections, blood group and HLA type.
- The potential to administer ante mortum agents to maintain the function of an organ where that is either local policy or in a particular case thought desirable.
- The procedure following donation and the follow up by the Donor Transplant co-ordinator.

At this point lack of objection to organ and tissue donation will be documented.

If the family retract lack of objection at any point the organ donation team will stand down.

The Donor Transplant co-ordinator will arrange the surgical team and operating theatre and ensure arrangements to transfer the patient to theatre are in place.

For lung donation it is helpful to know whether the planned withdrawal of treatment includes extubation, as equipment for re-intubation and bronchoscopy will be required once death has been certified.

Next of kin and family support will be offered according to the Critical Care Unit guidelines and UK Transplant Donor Family Care Policy.

*A Donor transplant co-ordinator will review the families understanding of the situation and discuss the process of retrieval, ante-mortem blood sampling, testing of blood samples, ante-mortem treatments designed to maintain the performance of organs and the post-mortem cold preservation where appropriate will be discussed.*

*If the family retract lack of objection at any point the organ donation team will stand down.*

# Role of the donor transplant co-ordinator prior to death of the donor

### For Category 1, 2, 5 and some category 4 donors

In this situation the co-ordinator as well as the surgical retrieval team are required to attend very promptly, most usually the Accident and Emergency department and less often-other departments in a hospital.

In this situation there is often very little time to acquire information. The co-ordinators assessment will be initially from Casualty staff and Paramedic records and medical history of particular relevance at this stage is previous malignancy, diabetes, hypertension and the documentation relating to the failed cardio-pulmonary resuscitation. An estimate of the likely warm ischaemia time is extremely important.

The national donor register will be checked to see if the potential donor was registered.

This information will be discussed with a Consultant in Transplantation for their opinion regarding suitability for organ donation. The potential for tissue donation should be explored with competant authorities.

If next of kin or family are present a verbal lack of objection will be obtained prior to cannula insertion and perfusion. If family members are not present cannulation can still be initiated while efforts are made to locate the next of kin. In this situation approval for the *in-situ* cooling process will have to be obtained from the Coroners Office by prior agreement or on a case-by-case basis. It is anticipated that the Human Tissue Act will clarify this area.

As soon as is practicable the co-ordinator will interview relatives. If they agree to consider organ donation a Donor transplant co-ordinator will discuss:

- Medical and social history, including completion of UK Transplant's Donor assessment documentation and General Practitioner Questionnaire.
- Ensuring that families are aware that some kidneys may be found unsuitable for transplantation post retrieval.
- The procedure following donation and the follow up by the Donor transplant co-ordinator.

At this point lack of objection to organ and tissue donation will be documented.

If the family retract lack of objection at any point the organ donation team will stand down and the cannula used to administer the cooling perfusate removed.

The Donor transplant co-ordinator will arrange the surgical team and operating theatre and will be responsible for the arrangements to transfer the patient to the operating theatre.

The next of kin and other family members will be offered support according to the Department guidelines and the UK Transplant Donor Family Care Policy.

*The Donor Co-ordinators prime purpose will be to gather information to allow clinicians to assess suitability the for non-heart beating organ donation.*

*Usually most critical is the potential donors past medical history as well as the documentation relating to the failed cardio-pulmonary resuscitation. An accurate estimate of the likely warm ischaemia time is extremely important*

*In the situation where approval of the in-situ cooling process has been obtained from the Coroners office and other competent authorities the team will initiate this.*

*If the family retract lack of objection at any point the organ donation team will stand down.*

# Consent

## For *in-situ* organ perfusion

It is not clear at the present time that consent is required for *in-situ* organ perfusion but it is certainly preferably commenced only after written consent being first obtained from next of kin. The forthcoming Human Tissue Act it is anticipated will clarify this area from a legal standpoint. The relatives are told that the purpose of the in-situ perfusion technique is to cool the organs within the body so that it may be possible to remove them later and use them for transplantation. This will give the next of kin more time to consider whether they wish to consent to organ donation.

Placing cannula for *in situ*-renal perfusion in the situation where there are no relatives available and the deceased's prior wishes are not known is possible and has been practised in some areas in United Kingdom for many years. In this situation consent for organ retrieval from the deceased is discussed with relatives when contacted as in the paragraph above. If consent is not obtained the process is stood down.

As discussed above it is probable that the forthcoming Human Tissue Bill will clarify the legal situation and if the final Bill were similar to the draft legislation it is likely would encourage the expansion of this opportunity to become an organ donor.

## For Organ retrieval

Commencement of retrieval will only proceed when the following conditions have been met:

1) Lack of objection is indicated by the next of kin.

2) Where appropriate the Coroner, or Deputy has given permission to proceed with organ retrieval.

3) Where appropriate the Coroner's Pathologist has given permission for organ retrieval and names the specific organs that can be removed.

## Next of kin

As a general guide, the legal next of kin of the deceased person, as defined by the Treasury Solicitor, are:

1) The legally married partner or close blood relative; son, daughter, mother, father, grandchild, brother, sister.

2) A legally adopted child has the same rights as if he or she had been born into the adoptive family.

3) A separated wife or husband has the same entitlement as existed before the separation, even if there has been a 'Deed of Separation'. Entitlement ceases, however, if there has been a 'Deed of Judicial Separation' as this has the same power as a Decree Absolute of divorce. However, for the purposes of this guidance, where spouses are separated, but not judicially, then consent shall not be obtained from the spouse. A divorced spouse has no entitlement.

4) Confusion may arise with any relationships involving 'step' relationships, including in law relationships, common-law, or same gender relationships and second-cousin relationships. Such a person cannot be defined as 'legal next of kin'. The Draft Human tissue Bill in Part 2 section 24 (4) gives a new list of "qualifying relationships" [5].

'Whilst for the purposes of this policy certain persons, including common law spouses, are not regarded as next of kin, wherever it is apparent that a close relationship existed with the deceased, it is always advisable in these circumstances to consult with them. If there is the potential for significant family dispute regarding consent the procedure is often abandoned.

Placing cannula for *in situ*-renal perfusion in the situation where there are no relatives available and the deceased's prior wishes are not known is possible and has been practised in some areas in United Kingdom for many years. In this situation consent for organ retrieval from relatives is discussed when they can be contacted. If lack of objection is not obtained the process is stood down.

# Diagnosis of death

A fundamental principle of organ donation is retrieval from a patient who has died. There is no statutory definition of death in English and Welsh Law. It is welcomed that the planned Human Tissue Bill [5] based on the consultation document Human Bodies Human Choices [6] is likely to provide a definition.

The Department of Health revised code of practice published in 1998 defined death as "the irreversible loss of the capacity for consciousness combined with irreversible loss of the capacity to breathe".

It seems logical that the key requirement is for the clinician certifying death to be confident that an interval has elapsed without cardiac output that is long enough to ensure that hypoxic injury to the cerebral cortex and brain stem has occurred. This must be such that the patient has suffered the irreversible loss of both the capacity for consciousness and to breathe.

As is the case when the diagnosis of death is made based on the absence of brain stem reflexes the clinician making the diagnosis will not be part of the organ retrieval team. However the retrieving surgeon needs to be confident that a competent clinician has established the diagnosis.

In the United States of America the Committee on Non-Heart-Beating Transplantation II in their publication Non-Heart-Beating Transplantation [1] "found that the interval of five minutes between the cessation of cardiopulmonary function and the declaration of death provided adequate assurance of the irreversible cessation of cardiopulmonary function, and satisfied the requirements of the Universal Determination of Death Act".

In hospital clinical practice in normothermic conditions and without the presence of agents that have been shown to offer a degree of cerebral protection there is rarely difficulty establishing the diagnosis.

*It seems logical that the key requirement is for the clinician certifying death to be confident that an interval has elapsed without cardiac output that is long enough to ensure that hypoxic injury to the cerebral cortex and brain stem has occurred such that the patient has suffered the irreversible loss of both the capacity for consciousness and to breathe*

*An interval of a minimum of five minutes is recommended.*

# Immediate post mortem management for renal or renal and liver donors

## For Category 1, 2 and 5 donors

Much the largest proportion of these donors will be from within the Accident and Emergency departments. Referrals to the transplant team will be made after the attending medical team has pronounced death. It will be the responsibility of the attending medical team to explain to the relatives that the patient has died. The time and date of the pronouncement of death will be recorded in the patient's notes.

External cardiac massage and ventilation with 100% oxygen can then be re-established where this has been agreed as the local protocol.

Non heart beating donor kidneys may be perfused and cooled *in-situ* using a double balloon, triple lumen intra-aortic catheter. The femoral artery and vein on one side is approached through a short groin incision and the double balloon perfusion catheter introduced into the aorta via a femoral arteriotomy. 100 mls of blood are taken for viral serology, biochemistry, tissue typing and toxicology. The balloons inflated and perfusion commenced. Some units prefer to instil radiographic contrast medium in the balloons in order to check that the catheter is correctly positioned for selected perfusion of the renal arteries. The system is vented by placing a foley catheter into the femoral vein at the groin. The kidneys are perfused with a total of 10-20 litres of hyperosmolar citrate solution cooled to 4 C. Each litre of perfusate has 5000units of heparin added. Some units additionally use a bolus of 1.5 mega units of streptokinase which at the outset of perfusion. Some units utilise cooling devices require additional ports to be inserted into the abdomen in addition to perfusion cannula

In Spain and parts of the USA, but not UK, cooling of the whole of the abdominal viscera of the cadaver is practiced when after failed cardio-pulmonary resuscitation large bore cannulae are inserted into major arteries and veins in the groin and connected to an extracorporeal cooling and oxygenation circuit. In this situation this allows family members to be contacted and informed of events and subsequently approach to consider organ donation. In Spain legislation also requires judicial approval to proceed.

The Draft Human Tissue Bill which it is intended will replace The Human Tissue Act of 1961 allows for persons having control of the management of the institution where the body is lying to take the minimum steps using the least invasive procedure necessary for preserving the body for use in transplantation. This authority would cease if it became established that consent for removal of a part for transplantation has not been, and will not be, given. If this act is passed in this form it will at the least clarify the legal situation.

For some category five donors it may be realistic to move to immediate organ retrieval and as for Category 3 donors the logistics of this will depend upon the availability of surgical staff and operating theatres as well as the need for relatives to be informed and register lack of objection.

# Immediate post mortem management for renal or renal and liver donors

### For Category 3 donors

The timing of retrieval after the diagnosis of death due to cardiac arrest is somewhat vexed. All Transplant authorities have recommended an interval to ensure brain stem death as well as cardiac standstill. In Pittsburgh an interval of two minutes has been adopted. The original Maastricht protocol had a ten minute interval however a period of five minutes is now accepted in primary legislation in the Netherlands.

This five minute period is in excess of the time the brain stem can survive in a situation of warm hypoxia and is the interval recommended by these guidelines.

### For Category 4 donors

Interventions to optimise organ viability in these individuals, who are legally dead and awaiting retrieval, do not differ at first principle from continuing artificial support whilst awaiting that retrieval, particularly if 'lack of objection' for donation has been recorded. Resuscitation manoeuvres, immediate transfer to the operating theatre and cannulation for cold perfusion could be accommodated without the need for any further legislation or guidelines. It would be mandatory however to keep the family informed and ensure their support for this course of action.

*Category 1, 2 and 5 donors*

*Referrals to the transplant team will be made after the attending medical team has pronounced death. It will be the responsibility of the attending medical team to explain to the relatives that the patient has died.*
*There will be no interventions for a period of five minutes.*
*External cardiac massage and ventilation with 100% oxygen can then be re-established.*
*Organs may be perfused and cooled in-situ*

*For Category 3 and 4 donors*

*There will be no interventions for a period of five minutes*
*Usually after that interval rapid retrieval is initiated, if this needs be delayed in-situ organ cooling can be considered*

*For all donors*

*Relatives need to be fully informed as early as is practicable and invited to register a lack of objection. Organ or tissue donation may be possible with consent to some but not all of the procedures.*

# Process of organ retrieval

## For abdominal organs

If asystole does not occur within 2 hours the liver retrieval maybe abandoned, although kidney retrieval maybe still possible after an interval of several hours.

Two approaches to achieve cold perfusion are used. Firstly to perform a femoral cut down and in situ perfusion with a short while later transfer to the operating theatre. The second approach is to combine the cannulation with the laparotomy. The latter approach is commonly used if livers and pancreas are retrieved, as portal perfusion is then possible. With the femoral cut down approach the donor is moved to theatre and retrieval performed within two hours.

A standard abdominal incision is performed and the abdominal cavity cooled with ice slush as soon as possible. For a kidney only retrieval these are removed and perfused. The kidneys are partially prepared to assess the quality of perfusion and back table perfusion continued until the effluent form the renal vein is clear and the kidneys appear uniformly perfused. Some practitioners advocate the use of streptokinase during the retrieval of organs from category one, two, three, four and five donors. In a small-randomised controlled study an improvement in viability characteristic of procured kidneys was demonstrated if a streptokinase pre-flush was used [7].

If the surgeon is retrieving liver and pancreas this should be done in the usual way after aortic and portal perfusion have been established. The first bag of low viscosity kidney preservation solution and the first bag of UW solution for the portal vein should contain heparin (20.000 IU). Care must be taken to avoid damage to variants in the vasculature as these aberrant vessels are more difficult to identify and easier to damage when pulse less. Probably this is best first performed with *in situ* perfusion of the kidneys continuing while the liver and pancreas are mobilised. To reduce liver congestion it may be useful to drain the IVC before aortic cannulation and some units utilise a fibrinolytic pre flush.

The conflict between the desirability of rapid surgical retrieving to minimise ischaemia time and the need to keep to a minimum the manipulation of pancreas for whole organ transplants proposes significant technical challenges.

The abdomen is closed and the operator tabulates the procedure and the organs removed in the patients notes for the Coroners pathologist.

## For lungs

If the withdrawal of treatment and cannulation and perfusion of the abdominal organs is to occur in the Intensive Care Unit the following procedure for non heart-beating lung donation will be followed and is carried out simultaneously with the cannulation and perfusion of the abdominal organs.

# Process of organ retrieval

1) *The Cardiothoracic retrieval team must be on site when treatment is withdrawn*
2) *Treatment is withdrawn*
3) *If asystole does not occur within 1 hour the lung retrieval will be abandoned*
4) *Asystole*
5) *Death certified by local medical staff*
6) *Stand off time as per local protocol*
7) *Rigid bronchoscopy is performed*
8) *Size 16-Foley catheter is inserted into the distal trachea*
9) *Patient is reintubated with 6mm ET tube*
10) *The lungs are inflated, the ET tub is removed and the foley catheter is placed in the larynx*
11) *The family can return once this and the cannulation and perfusion of the abdominal organs are completed. The foley catheter is not visible.*
12) *The patient is transferred to the operating theatre*
13) *Time between asystole and cold flush of the lungs in theatre should be less than 90 minutes and ideally less than 60 minutes*
14) *Sternotomy performed*
15) *Assessment of lungs*
16) *Pulmonary artery opened and clot removed*
17) *Lungs are flushed*
18) *Heart lung block is removed. If there is no consent for heart valve donation the heart will be put back into the body*
19) *Retrograde flush of the lungs on the back table and packed for transportation*
20) *Time from sternotomy to the end of the retrieval will be approximately 1 hour*

*There is more than one possible approach to achieve cold perfusion of abdominal organs.*

*Some practitioners advocate the use of streptokinase during the retrieval of organs from category one, two, four and five donors*

*If the surgeon is retrieving liver and pancreas this should be done in the usual way. Probably this is best first performed with in situ perfusion of the kidneys continuing while the liver and pancreas are mobilised. To reduce liver congestion it may be useful to drain the IVC before aortic cannulation and some units utilise a fibrinolytic pre flush.*

*The conflict between the desirability of rapid surgical retrieving to minimise ischaemia time and the need to keep to a minimum the manipulation of pancreas for whole organ transplants proposes significant technical challenges*

*The procedure for non heart-beating lung donation is carried out simultaneously with the cannulation and perfusion of the abdominal organs.*

# Preservation of organs following non heart beating organ donation

The Organ Preservation, Ischaemia/Reperfusion Discussion Forum of the BTS will be producing guidelines for preservation in the future and so detailed recommendations may well change. In the section of the British Transplantation Society's website relating to this forum are collected recent key references to research in this area.

Two types of hypothermic preservation solutions are commonly used. A normothermic haemoglobin based solution is in development.

The donor is initially perfused with large volumes of hypothermic flush. EuroCollins, Marshalls or HTK solution can be used in this situation, as they are all relatively inexpensive. After retrieval the kidneys, which have already been damaged by warm ischaemia, should be flushed and stored either in University of Wisconsin (UW) machine preservation, or HTK solution. Some debate exists as to the merits of high viscosity solutions and costs too have been raised as a concern, however compared to the consequences of transplanting a non-viable kidney the cost is justified.

The potential contribution of machine perfusion of kidneys retrieved from non-heart beating organ donors is not clear [8]. It does allow the possibility of measuring a number of markers that may correlate with function. Whether the process itself allows an extension of the acceptable cold ischaemia time or improves initial function is not yet established. A report on the value of machine perfusion in kidney transplantation, has been commissioned by the Department of Health [9]. This concludes that the short-term cost/benefit of machine perfusion did not justify its use, but that there may be sufficient cost/benefit if long-term outcomes are considered - but the evidence base is incomplete. This meta-analysis modelled the effects of machine perfusion on renal graft survival in non-heart beating and heart-beating donors groups. They predicted a 20% reduction in the instance of delayed graft function, and a 2-3% improvement in 10-year graft survival could be gained through machine perfusion. Their analysis of cost/benefit of machine pulsatile perfusion was extended from time of transplant to 10 year survival and concluded where delayed graft function has a higher incidence, such as in kidneys retrieved from non-heart beating donors, the combined benefit of reduced delayed graft function and improvements in 10 year survival rates may well make machine perfusion a cost effective option in the long term. The authors concluded that more research is necessary to determine whether machine perfusion can produce significant clinical and economic benefit to organ preservation.

As in heart beating organ retrieval the standard solution used for liver and pancreas cold preservation is UW solution though low viscosity solutions such as HTK have been proposed as being more appropriate.

There is ongoing research activity to try to minimise the degree of ischaemic injury [10, 11,12]. There is substantial research interest in the possibility that normothermic preservation may result in less injury to livers [13]. This is particularly important in the setting of non-heart beating donation.

*Kidneys which have already been damaged by warm ischaemia should not be stored in Marshalls or EuroCollins solution*

*The potential contribution of machine perfusion of kidneys retrieved from non-heart beating organ donors is not yet clear*

*There is substantial research interest in the possibility that normothermic preservation may result in less injury to livers.*

# Viability testing

A major limiting factor to the widespread adoption of a non-heart beating organ donation and transplantation is the uncertainty regarding the function of the graft once transplanted. Delayed function, rejection and extended hospital stay are all a concern with non-heart beating organ donation but primary non-function has more significant consequences. Primary non-function is especially important for the recipient of a life-sustaining organ such as a liver or lung. The need to minimise the cold ischaemia time reduces the time available for viability testing.

The principal purpose of viability testing is to reduce primary non-function. Non-heart beating donor kidneys are prone to acute tubular necrosis. Viability testing should therefore focus upon determining the severity of injury to the tubules and supporting microcirculation. Evidence also suggests that the damage the kidneys sustain is not necessarity bilateral, therefore one could not assume that if one kidney presents as being viable the other also falls into this category.

## Risk factors for renal primary non-function

Donor factors: Age >60; Serum Creatinine >150, Warm Ischaemic time >45 minutes, Cold Ischaemic time >22 hours (ice storage). The efficacy of cooling and rate of cooling have all been shown to be associated with higher rates of primary non-function.

Recipient factors: Sensitised or re-transplanted patients, early rejection episodes and early expose to nephrotoxic agents, including cyclosporin and tacrolimus.

At present time though there is no conclusive evidence as to the best viability tests to use. There are advocators of visual inspection, perfusion characteristics on machine perfusion and enzyme levels in the perfusate [14, 15]. Whatever method is used by the centre careful audit is required to maintain good results and if the primary non-function is greater than 5% the measures used for testing viability must be modified.



## Viability Criteria (Newcastle 2001)

| | |
|---|---|
| Flow | > 23ml/100g |
| GST | < 200 IU/100g |
| Temperature (°C) | < 14 (surface temperature)<br>(five time points) |
| Wt increase (%) | 10-25 % (relative contraindication) |
| Index (ml/min/100g/mmHg) | >0.4 (most important) |
| Perfusion pressure (mmHg) | <60 mmHg |
| Perfusion fluid | Belzer UW with 1000u heparin per litre |
| Donor pre-treatment | Heparin and Streptokinase |

*continued on page 18*

# Viability testing

Additional points:

1) Younger donors with shorter warm ischemic times have better outcomes independent of the above variables.
2) Retrieval should be within ninety minutes of perfusion.
3) Cold ischemic time must not exceed 24 hours.
4) The position of the catheter balloons should be checked at retrieval.

Objective assessment of texture, colour, consistency and perfusion effluent on the back table are important parts of the assessment.



*Primary non-function has significant adverse consequences. These are especially severe for the recipient of a life-sustaining organ such as a liver or lung*

*The principal purpose of viability testing is to reduce primary non-function*

*At present time though there is no conclusive evidence as to the best viability tests to use*

# Recipient selection and laboratory protocol

Given the possibility of an inferior (initial) performance of kidneys retrieved from non-heart beating donors some argue that these organs should be reserved for candidates for whom the consequences of prolonged delayed graft function are not especially serious or who do not benefit particularly from a large nephron mass.

For recipients of other organs in part because of the lack of other options the allocation to any particular recipient is usually governed by local clinical imperatives.

Kidneys (and other organs from non-heart beating donors) are currently in the UK allocated within the pool of potential recipients registered with the retrieving centre, in part to minimise the length of cold ischaemia time. In the future it may be appropriate to allocate within a renal sharing alliance waiting list. This will depend at least in part on local geographical considerations. Units at present in general either allocate the organs using the same criteria as organs retrieved from heart beating donors or alter the allocation rules to favour candidates who are less likely to receive an offer via the national matching scheme.

Organs retrieved from non-heart beating donors are at risk of warm ischaemic injury during the interval from withdrawal of full support and cardiac arrest for category 3 donors and during unsuccessful resuscitation attempts for other categories of donors. Organs retrieved from heart beating donors do not experience this initial warm ischaemic injury.

Cold ischaemic injury that occurs in the interval between retrieval and re-implantation and is usually measured in several hours is likely to be particularly deleterious to the function of organs retrieved from non-heart beating donors.

In order to try to minimize the duration of this interval it may be appropriate to organize a "fast-track" method of handling recipients. Potential ways to reduce the interval include pre-retrieval HLA typing, for organs where that is part of the allocation algorithm. The selection of recipients who are unlikely to be sensitised to mismatched donor antigens and hence demonstrate a positive current cross match (where that is performed) or calling up potential recipients as reserves where the first choice is at high risk of prior donor specific sensitisation. These strategies will require access to efficient and high quality HLA typing by the most accurate methods.

One algorithm and management protocol for allocation of kidneys that is similar to the national scheme is included as appendix A. Another approach is to allocate one kidney from a donor by rules similar to the national allocation rules, but the other kidney by rules designed to favour candidates who have demonstrated by spending by a long period on the waiting list that they are less likely to receive a kidney from the national pool [16]. An example of such a scheme is shown in appendix B.

Units are likely to adopt strategies and allocation rules that are different to take into account local geography and established practice.

*Renal units in general either allocate the kidneys using the same criteria as organs retrieved from heart beating donors or alter the allocation rules to favour candidates who are less likely to receive an offer via the national matching schemes.*

*For recipients of livers and lungs in part because of the lack of other options the allocation to any particular recipient is usually governed by local clinical imperatives.*

# Initial immunosuppression and care

## Renal transplant recipients

The Health Technology Appraisal published in 2004 by The National Institute of Clinical Excellence on Immunosuppressive Therapy post Renal Transplantation did not consider recipients of non-heart beating organs and in our view the recommendations should not be applied to this group.

These organs are likely to have experienced an increased length of warm ischaemia compared to organs retrieved from heart beating donors. The length of warm ischaemia influences the likelihood of delayed graft (and primary non) function. It is logical to try to minimise further nephrotoxic injury to the graft. To delay the introduction of nephrotoxic immunosuppression until the transplant is functioning or to avoid nephrotoxic immunosuppression is practiced my many centres. There are limited published results to guide practice.

In a small-randomised trial of 29 patients micro emulsion ciclosporin was compared to tacrolimus in recipients of renal transplants from non-heart beating donors [17]. Unfortunately despite randomisation the degree of DR mismatch was uneven as was the proportion of controlled and uncontrolled donors. There were no clinically critical differences in outcome. The majority of the recipients of non-heart beating kidneys reported in the literature have received ciclosporin. The optimal immunosuppressive strategy remains to be established.

Initial treatment with IL-2 receptor blockers, prednisolone and mycophenolate mofetil with the delayed introduction of a calcineurin inhibitor when there is either graft function with a creatinine below an arbitrary level of say 350 micromol/l or there is evidence of rejection is practiced by some units.

Systemic heparinisation is sometimes employed particularly if there is no immediate graft function or the donor was category one, two, four or five. When the donor was from one of these categories protracted prophylactic antibiotic cover including for anaerobes for three days post surgery is recommended.

It is not clear whether recipients of kidneys from non-heart beating donors experience a significant excess of rejection. It is certainly more difficult to diagnose if there is delayed graft function. Weekly biopsy in the presence of delayed graft function is recommended. Histological appearances of the graft particularly of the blood vessels are often atypical. Vascular changes that can mimic "vascular rejection" are not that uncommon.

## For recipients of other solid organs

The world wide experience in recipients of liver, lung and pancreas transplants is still small. It is not yet clear if there are any complications that are peculiar to recipients of organs from this source. Neither is it clear what is the frequency of complications compared to that seen in recipients of organs from heart beating donors.

Clearly primary non-function in recipients of liver or lung transplants is extremely serious, as would be an increased incidence of certain other complications such as late hepatic artery thrombosis.

*It is logical to try to minimise further nephrotoxic injury to the renal transplant.*

*There is limited experience in recipients of liver, lung and pancreas transplants. It is not clear if there are any complications that are peculiar to recipients of organs from this source.*

# Graft outcome after non-heart beating organ retrieval

## Renal transplants

Summarising the predicted outcome following kidney transplantation with kidneys retrieved from non-beating donors is not straightforward. The series have usually been reported from single centres and involve relatively small numbers of patients. The results may not be easily reproduced in another service. Inevitably the series with the longest follow up are from grafts performed some while ago. During the interval immunosuppressive strategies have changed, the accuracy of HLA matching and HLA specific antibody screening improved and patient co-morbidity better defined. Patients will have been managed with a higher dose of dialysis, with improved correction of anaemia and hyperparathyroidism all of which may be expected to improve outcome. In contrast the average age of patients starting dialysis's has increased significantly with inevitable effects on co-morbidity and predicted longevity.

The outcome of 122 recipients of kidneys from non-heart beating donors were compared the same number of recipients of kidneys from heart beating donors with up to 15 years follow up [18]. The rate of delayed graft function was higher at 48 percent in the first compared to 24 percent in the latter group. The rate of primary non-function was not significantly different at 5.7 and 4.9 percent. Graft survival counting recipient death as graft failure was 74 and 76 percent at five years and 64 and 61 percent at 10 years. The paper summarises the results of the largest comparable reports and table 1 is principally adapted from this publication.

United Kingdom transplant have published a comparison of the outcome of first cadaveric kidney only transplants retrieved from non-heart beating and heart beating donors encompassing the



Table 1

**Studies of Kidney Transplantation From Donors Without a Heartbeat**

| Reference | No of Transplantations From Donors Without a Heartbeat | First Year of Program | Duration of Study | Matched Patients | Graft Survival | | |
|---|---|---|---|---|---|---|---|
| | | | | | Time After Transplan-tation | Donors With a Heartbeat | Donors Without a Heartbeat |
| | | | yr | | yr | Percent | |
| Wijnen *et al* [19] | 57 | 1980 | 12 | Yes | 5 | 55 | 54 |
| Gonzalez Segura *et al* [20]† | 52 | 1985 | 10 | No | 5 | 77 | 68 |
| | | | | | 9 | 66 | 50 |
| Pacholczyk *et al* [21] | 76 | 1986 | 9 | Yes | 1 | 90 | 82 |
| Balupuri *et al* [22] | 47 | 1988 | 10 | No | 5 | 83 | 88 |
| Sanchez-Fructuoso *et al* [23] | 95 | 1989 | 10 | No | 5 | 84 | 83 |
| Cho *et al* [24] | 229 | 1994 | 2 | No | 1 | 86 | 83 |
| Sanchez-Fructuosa *et al* [25] | 188 | 1995 | 7 | Yes | 7 | 87 | 93 |

*† The survival rates were estimated by Kaplan-Meier analysis.*

*continue overleaf*

# Graft outcome after non-heart beating organ retrieval

period 1994 to 2000 [26]. Although the number of kidneys retrieved from non-heart beating donors is small at 172 compared to 8046 in the other group the data show an increased early graft loss in the non-heart beating group then parallel rates of graft was over the first year. One-year transplant survival was not significantly different at 82 versus 85 percent where there was a non-heart beating versus heart beating donor.

## Pancreas transplants

In one series of 18 simultaneous kidney pancreas transplants performed between 1993 to 1999 when pancreata were retrieved from category 3 non-heart beating donors were compared in a single centre study to 339 recipients of organs for heart beating donors. There was a higher rate of enteric conversion (32% versus 13% $p < 0.01$) for recipients of pancreas from non-heart beating versus heart beating donors. No difference in patient (100% versus 95.4%) or pancreas (87.4% versus 86.5%) survival was seen [27].

Non-heart beating donors may prove to be a particularly valuable source of cells for isolated islet transplantation.

## Liver transplants

The donor organ shortage of end-stage liver disease is a particular serious problem given the lack of efficacy of any alternatives. However re-perfusion syndrome and primary non-function in the transplant recipient is extremely serious and in the latter situation unless a replacement graft can be found promptly is invariably fatal. In addition the biliary tree is especially at risk of ischaemic injury resulting in both early and late complications.

At present the only donors that can be used for liver transplantation are those that have minimal warm ischaemia and therefore are from the Maastricht categories three and four.

In an ITU setting eight livers were retrieved from non-heart beating donors where cardiac arrest occurred after a short interval, 3 to 27 minutes after ceasing artificial ventilation. Patient and graft survival are 100 percent at a mean of 18 months follow up [28]. The results of 144 recipients of livers from non-heart beating donors performed between 1993 and 2001 were compared to the contemporaneous 26856 liver transplants from heart beating organ donors registered on the United Network of Organ Sharing database in the USA. One-year graft survival was 63.3% and 80.4% (non-heart beating versus heart beating donors p= 0.003). Three-year graft survival was also poorer in recipients of organs from non-heart beating donors at 63.3% and 72.1% (p= 0.012). Recipients of a non-heart beating graft had a greater incidence of primary nonfunction (11.8% versus 6.4%, p= 0.008) and retransplantation (13.9% versus 8.3%, p=0.04) compared to recipients of livers from heart beating donors [29].

In a single centre study biliary complication occurred in five out of 15 (33%) recipients of liver transplants from non-heart beating donors and in 19.2% of recipients of livers from heart beating donors (n=221,p<0.01) [30]. It is of concern that half of these biliary complications were ischaemic cholangiopathies that are likely to lead to secondary biliary cirrhosis and may require regrafting.

Many groups are actively exploring this donor source at present and it may make a significant contribution to the donor pool in the future [31].

# Graft outcome after non-heart beating organ retrieval

## Lung Transplantation

Lung transplantation is a lifesaving therapy for selected patients with end stage lung disease, but its application is severely constrained by suitable donors. Within the UK only 20-30% of heart beating organ donors are suitable for lung donation, this is in stark contrast to the retrieval rate for abdominal organs.

The lung may be the ideal organ for non-heart beating organ donation because unlike other solid organs, the lung does not rely on perfusion for parenchymal cellular respiration to occur. Tissue levels of high-energy nucleotide phosphates have been demonstrated to remain near normal up to four hours after the cessation of circulation provided the lungs remain inflated with oxygen.

The technique for the retrieval of lungs from a non-heart beating organ donor was developed in the animal model. Its success relies upon rapid bilateral chest cavity flushing or topical cooling to induce hypothermic conditions post cardiorespiratory arrest, the use of heparin and intravascular flush via a pulmonary artery catheter. This technique has protected the function and morphology of cadaver lungs, which are then suitable for transplantation.

The agonal period in humans is never as controlled as in a laboratory model and organ viability is often compromised to a degree that is difficult to determine. Work is therefore continuing in to develop a ventilation and perfusion assessment technique for non-heart beating donor lungs, which could differentiate between those lungs with good and poor function post-transplantation.

Other work in the animal model has demonstrated lungs from non-heart beating organ donors can provide adequate pulmonary function with careful manipulation of the recipient upon re-perfusion.

Using similar technique that described above a Swedish group has recently described lung retrieval from a non-heart-beating donor. The donor died after failed cardiopulmonary resuscitation following an acute myocardial infarction in a cardiac intensive care unit. Three hours post death and initial cooling the heart lung block was removed. The right lung was transplanted and has demonstrated good function at five months follow up [32].

As many retrieval units are in the process are developing non-heart beating protocols, the potential for lung donation should not be overlooked [33].

*Summarising the predicted outcome following kidney transplantation with kidneys retrieved from non-beating donors is not straightforward. It is anticipated that the risks of primary non-function, delayed graft function are increased and there is a reduced graft survival.*

*In the UK there is an increased early renal graft loss in the non-heart beating group then parallel rates of graft was over the first year. One-year transplant survival was not significantly different at 82 versus 85 percent where there was a non-heart beating versus heart beating donor.*

*The experience of recipients of other solid organs is presently small and it is difficult to draw meaningful comparisons.*

*Given the shortage of solid organs for transplantation the most appropriate comparison may be with the experience of patients who do not receive an organ rather than with that seen after receiving an organ from a heart beating cadaveric donor.*

# Informing the Recipient Population

As the shortfall between the number of individuals placed on organ transplant waiting lists and the number of cadaveric organ donors grows there has been a progressive interest in attempting to retrieve organs from so-called marginal or extended donors. These are donors who in the recent past would have been considered unsuitable for organ donation because of medical co-morbidity. The field is changing rapidly but there is information allowing some predictions to be made about the likely difference in outcome between an "ideal" cadaveric donor and less than ideal donors.

By most criteria non-heart beating donors would be considered non-ideal. On average deceased organ donors are less ideal than a live donor where that is an option. Even among live donors there is clearly a graduation from what may be considered the perfect donor such as an identical twin, an option available only to a very small number of people.

Many clinicians and patient groups feel that as the outcome following non-heart beating donation is on average poorer compared with that seen with the average deceased brain dead donor, the non heart beating origin of the kidney transplant should be discussed with the intended recipient. This is in the setting where there are other options for life sustaining therapy such as dialysis. These discussions are far from strait-forward, as for any individual there is a need to quantify the degree of "risk" associated with each course of action, in a situation where such quantification is almost impossible.

Where the organ is the only life sustaining treatment then the patient's and medical team's options are clearly greatly constrained.

Given that admission for such a procedure is always an emergency and that often this occurs at unsocial hours to inform the patient group in good time about the potential for receiving an organ from a non-heart beating donor is good practice. To have a separate list of individuals for whom medical staff and the patient agrees that receiving a non-heart beating kidney would be a good option is also good practice. In Appendix C is one such patient information leaflet for potential renal recipients that may be used as a template to guide local practice.

*Many clinicians and patient groups feel that the outcome following non-heart beating donation is significantly poorer compared with the average cadaveric brain dead donor and that the origin of the kidney transplant should be discussed fully with the intended recipient. Informing this discussion will be the "Maastrich" category of the donor.*

*Where the organ is the only life sustaining treatment then the patient's and medical team's options are clearly greatly constrained.*

# Staffing implications

## Donor transplant co-ordinators

In order to facilitate non-heart beating organ donation Donor transplant co-ordinator teams must ensure they can be responsive to the needs of the Accident & Emergency Department or Critical Care Unit.

In programs offering in-situ perfusion co-ordinators are often required to attend the Accident and Emergency departments within 15-20 minutes of being contacted.

Strategies that are currently in place to facilitate non-heart beating organ include; in-house Co-ordinators based in Accident & Emergency departments or specific hospitals, as well as a second on Call Service for Non Heart Beating Organ donation.

In some centres, two donor transplant co-ordinators attend a referral. One co-ordinator's responsibility is to support and inform the family and staff within critical care unit and one to organise the logistical aspects of organ retrieval.

## Intensive care departments

The process of organ retrieval ought not impinge on clinical care or significantly affect staff numbers. The time devoted to staff development and education as well as counselling is however significant and consideration should be given to staff expansion of a nominated trained individual to carry out this role. This may well be an individual from an intensive care nursing or a transplant co-ordinator background.

## Transplant surgical staff

On call surgical teams for organ retrieval from non-heart beating donors may need to attend Accident and Emergency departments at short notice in order to place perfusion cannula. Similar to the co-ordinators availability within 30 minutes travel in time to the main Accident and Emergency source may be necessary. Again similar to the co-ordinators retrieval from patients on intensive care units may demand long periods in attendance at the hospital site during the agonal interval. For logistic reasons it may be sensible to declare an upper time limit for such a wait.

The successful retrieval from a non-heart beating donor may pose a significant logistic challenge if two kidneys, the liver and possibly other solid organs are retrieved in order to ensure adequate staff to implant recipients in a timely fashion.

## Operating theatre personnel

Rapid access to operating facilities is mandatory to allow the prosecution of a successful non-heart beating donor program. This is true both for organ retrieval and implantation. The retrieval from a cadaver without a heartbeat who is not ventilated is different to retrieval from a heart-beating donor. Support and education to operating theatre personnel should be available, probably best delivered by the transplant coordinators.

# Staffing implications

## For laboratory

No single Histocompatibility and Immunology staff member should attempt to investigate an import/local donor and an asystolic donor at the same time. Experience has shown that the workload in this situation is just manageable but time is fully committed and has to be tightly managed. This is not appropriate to the situation, which requires focused effort for the production of high confidence and timely results. The primary person on-call should have a back up.

## Inpatient ward areas

Kidneys retrieved from non-heart beating donor's have an increased likelihood of primary non and delayed graft function. Recipients will be expected to have an increased need for dialysis support and longer in patient stays that will have to be met from the acute transplant ward resources.

*It is much less easy to plan retrieval from non-heart beating donors in an active programme a back up retrieval team may be required.*

*In a program offering in-situ organ perfusion following unexpected cardiac arrest there are considerable burdens placed on the retrieval team who need to attend a short notice.*

*Rapid access to operate facilities is mandatory to allow the prosecution of a successful non-heart beating donor program.*

*No single Histocompatibility and Immunology staff member should attempt to investigate an import/local heart beating donor and a non-heart beating donor at the same time. The primary person on-call should have a back up.*

# Author's potential conflicts of interest

***Dr C G Newstead*** has received multiple honoria for lectures and teaching as well as expenses for travel and accommodation to attend scientific meetings principally from Fujisawa, Novartis, Roche and Wyeth. He has received Honoria for contributions to advisory boards for Roche and Wyeth, but non-since appointed chair British Transplantation Society Standards Committee. Research and that of collaborators has been in part sponsored by the above named companies as well as the Yorkshire Kidney Research Fund, Medical Research Council, Ipsen International, Jensen-Cilag, Alpha Blood Products, Baxter Healthcare and Biotrin International

***Dr D Bell*** none declared.

***Mr N V Jamieson*** has received honoria for lectures and expenses for travel and accommodation to attend scientific meetings from Fujisawa, Novartis, Sangstat, Johnson and Johnson and Wyeth and has received Honoria for contributions to advisory boards for Wyeth.

***Mr D Talbot***: has received multiple honorary for lectures and teaching. He has also received travel tickets and accommodation to attend various meetings principally from Fujisawa, Novartis, Roche and Wyeth. Research sponsorship has come from the Northern Counties Kidney Research fund, the Special trustees of the Newcastle Hospitals NHS Trust, Fujisawa, Roche and Novartis.

***Dr P Murphy*** none declared.

***Miss L Robson*** none declared.

***Mr S Willis*** none declared.

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# Appendix A

Recipients listed at UKT for NHBD donors must:

1) Have a well-documented clinical history
2) Have been screened for HLA specific sensitisation in accord with BTS guidelines (one sample every 3 months)
3) Must be either unsensitised or have a residual reaction frequency of <10%
4) Adult patients registered on Local Centre waiting list (non-heart beating donor kidneys are rarely allocated to recipients outside of the retrieval centre).
5) Known to have indicated that willing to accept non-heart beating donor kidney (to be actioned after an interval to allow people to organize mail shot and replies to be collated)

**Step 1**

Donor HLA typed on peripheral blood after consent from relatives (virology testing, ABO group et cetera) (4-4.5h)

**Step 2**

Matching run performed by UKT using the following eligibility criteria and sort order (after appropriate implementation and testing):

1) Adult patients registered on Local Centre waiting list
2) Known to have indicated that willing to accept non-heart beating donor kidney
3) No donor relevant HLA antibodies known
4) 000 HLA A, B and DR mismatch grade
5) Minimum
   Recipient age donors age minus ten years (points system to tie break)
6) Usual matching rules for other mismatch grades (e.g., homozygotes first, HLA mismatch grade, points system to tie break)
7) Minimum
   Recipient age donors age minus five years
8) Recipients all ages

**Step 3**

Sort order notified by UKT to transplant team on call (note this may be prior to organ retrieval).

If top two candidates are registered as unsensitised.

For top two potential recipients transplant team liaise with relevant renal medicine staff about current suitability for transplantation. Check made at this time that no known sensitising events since last antibody screen.

If one or more of top two candidates' medically unsuitable move to candidate three and so on.

Decision made whether appropriate to call in recipients prior to retrieval made. This will depend upon how likely it is predicted that the retrieval may be unsatisfactory.

Otherwise call in candidates when organs retrieved.

When patients contacted check made at this time that no known sensitising events since last antibody screen.

If one of or more of top two candidates does not meet criteria of no known sensitising event, serum screen negative or if serum screen positive but and known more than 0% residual PRA then a back up candidate is nominated from sort list in order up to a maximum of four total potential candidates for two kidneys.

For back up recipients transplant team liaise with relevant renal medicine staff about up to date suitability for transplantation. Check made at this time that no known sensitising events since last blood sample.

If one or more back up candidates unsuitable move to next candidate and so on.

Decision made whether appropriate to call in recipients prior to retrieval made.

This will depend upon how likely it is predicted that the retrieval may be unsatisfactory. Otherwise call in candidates (and back ups) when organs retrieved

When patients contacted check made at this time that no known sensitising events since last blood sample.

**Step 4**

From results of step 3 perform crossmatches with selected recipients and back ups where nominated using according to locally agreed practices (2- 3h). Note crossmatch can take place prior to organ retrieval.



If historic peak or current positive cross match, recipients eliminated from consideration.

**Step 5**

Call in selected crossmatch negative recipients and repeat crossmatches with current sera (2-2.5h)

Or if decision made to call in prior to retrieval or prior to result of historic and current sera cross match known run cross match versus time of transplant sera when available. (2-2.5h)

Estimated total laboratory time ~ 8-10h

# Appendix B

All blood group compatible patients to be considered

Exclude patients whose recorded unacceptable antigens are shared by the donor.

Length of time on waiting list (latest listing excluding suspensions of > 6 months)

| Days | Points |
|---|---|
| 1100-1500 | 5 |
| 1501-2000 | 10 |
| 2001-2400 | 15 |
| 2401-2774 | 20 |
| >2775 | 25 |

**1) Previous transplant?**

a. Yes 0

b. No 5



**4) Age**

| Age | Points |
|---|---|
| < 40 | 10 |
| 41-60 | 5 |
| > 60 | 0 |

**5. Matchability score**

| Matchability score | Points |
|---|---|
| 9-10 | 10 |
| 7-8 | 8 |
| 5-6 | 5 |
| 3-4 | 3 |
| 1-2 | 0 |

The kidney is allocated to the recipient with the highest score. In the event of a tie subtract one point for each mismatched HLA antigen.

# Appendix C

**Important Information for Patients Awaiting a Kidney Transplant**

## Non Heart Beating (NHB) Organ Donation

As you know the demand for kidney transplantation in the UK is greater than the current supply of organs available. The Department of Health is implementing several initiatives to improve this situation.

These include:

- Making more direct appeals for people to carry donor cards and use the organ donor register.
- Increasing the number of transplants from live donors.
- Increasing the number of 'non-heart beating organ donation programmes'.

## What is a Non Heart Beating Organ Donation programme?

They are three methods of kidney donation within the United Kingdom.

**Living-donor organ donation.** In this situation a blood relative or someone who is emotionally related to the recipient volunteers to be a kidney donor.

**Organ donation after brain death.** This is often as a result of a head injury or stroke causing damage to the brain. If injury occurs to a vital area of the brain called the 'brain stem'; that patient can never regain consciousness or breath again and within hours their heart will stop beating. If tests conclude that death has occurred consent for organ donation is discussed with the family.

**Non-heart beating organ donation.** When non-heart beating organ donation takes place the donor has been declared dead following the absence of breathing and a heartbeat.

Several Transplant Units in the United Kingdom are developing a Non-heart beating Organ Donation programme. Although this will be a new development it is not a new idea. This method of organ donation has been used successfully in North America, Japan, Europe and three centres within the UK for many years.

**Receiving any kidney transplant carries certain risks.** These include those due to the actual operation, the possibility of the transfer of infection from donor to recipient and the anti-rejection medication. All kidneys offered for transplantation also experience some degree of damage. This is due to events prior to donation, the operation to remove the kidney, and the length of time the kidney is stored before it can be transplanted.

**Special risks with non-heart beating organs.** The major difference between kidneys donated from non-heart beating organ donors and other organ donors is the function of the kidney in the early days after the transplant. Usually these kidneys do not work straight away. This delay in function can last for days or weeks after the transplant operation. The recipient is required to continue with dialysis for a while after transplantation. Unfortunately it is difficult to predict the speed of recovery of the kidney.

Rarely the kidney never regains function. This can occur with any transplanted organ. The consequence of this is the disappointment of having undergone an operation that has been unsuccessful and the potential for your body to produce antibodies, which can make finding another transplant more difficult.

## Approximate Summary of Expected Results

**Approximate Summary of Expected Results**

| | Percentage Never functioning | Percentage with delayed Function | Percentage Graft survival 1 year | Percentage Graft Survival 5 year |
|---|---|---|---|---|
| Live related | 0 | 1 | 98 | 85 |
| Organ donation after brain death. | 2 | 20 | 90 | 75 |
| Non-Heart beating | 3 | 80 | 85 | 70 |

As you can see the kidneys donated from non-heart beating organ donors have a small increased risk of never functioning and a distinct increased risk of delayed function compared to kidneys donated from brain dead organ donors. The long-term results are similar.

The purpose of this document is to provide you with information so you can discuss with your relatives and the renal team whether you would consider having a non-heart beating Kidney transplant.

This development will not change your chances of receiving a kidney from the usual National Allocation System. But it will increase the chances of you receiving a kidney transplant sooner. This is because at present Kidneys donated from non-heart beating donors within the local region will only be used for patients on the local waiting list.

In order to keep the time between removing the kidney and transplantation to a minimum it is helpful if the Renal Transplant Unit are aware of those patients who would and those who would not accept a kidney from a non-heart beating organ donor.

**If you would accept a kidney from a non-heart beating organ donor could you please return the enclosed authorisation slip, which also asks for up to date contact details.**

**If you do not return the authorisation slip we will assume you do not want to be considered for this type of transplant.**


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