



INTRODUCTION

Organ transplantation is one of the greatest success stories in modern medicine. Through organ donation patients with life threatening illnesses can look forward to a new lease of life. For heart and liver recipients it is literally the difference between life and death. For kidney transplant recipients the quality of life improves dramatically and transplantation is the most cost effective way of treating end-stage kidney disease, not to mention the improvement in life expectancy.

However the demand for organs far exceeds supply throughout the world. And while living related transplantation has increased it has risks for the donor and is not a viable option for most organs. Sadly deceased donation has been decreasing in South Africa despite the criteria and methods for donation being expanded. Action needs to be taken to address this problem and begins with the education of health professionals such as yourselves.

The purpose of this chapter is not to teach you how to do a transplant, although an overview of the process is given. Rather emphasis is made on how to assess patients at the end of life and the correct processes to follow. It is these crucial steps that ensure opportunities for organ donation are maximized and empower you as doctors to be knowledgeable advocates for transplantation.

POTENTIAL DONORS – WHO CAN BE A DONOR?

All certified brain dead patients, *and patients in whom there is no chance of survival upon planned withdrawal of life support*, can be organ donors. Typical causes of death include traumatic head injuries, sub-arachnoid

haemorrhage, cerebral hypoxia, fat/air embolism or primary brain tumour.

Ideally the donor should be under 70 years of age, have no serious systemic diseases, no serious infection and no malignancy (aside from primary brain tumour). However these criteria have been relaxed given the good results shown in recipients of organs from *extended criteria donors (ECD)*. Therefore in the modern era organs will be considered for transplantation if organ function is preserved even in donors with systemic disease e.g. hypertension or diabetes and regardless of age.

Donation after circulatory death (DCD) has allowed organ donation to take place in donors where the strict criteria for brain death are not met. Medically the patient is assessed as having no chance of recovery and together with the family the decision is to withdraw futile intensive care support. In this setting it is possible to donate all organs except the heart, as upon withdrawal of support and cardiac arrest the patient can, after 5 minutes, be certified dead. The transplant team is required, prior to this, to be in theatre and ready to operate immediately in order to limit the warm ischaemic damage which occurs in this type of donation. Logistics are challenging and while results are not quite as good as donation after brain death they are still much better than no transplant at all.

If there is any doubt about whether a donor is suitable there is always a transplant co-ordinator on call who will be only too pleased to offer advice. Always err on the side of considering donation.

In Canada it is a legal requirement for any doctor involved in certifying death or planning withdrawal of life support to discuss the case with the transplant

co-ordinator and document the discussion in the notes, so called "required referral". South Africa has no such policy but it is good clinical practice.

WHAT CAN BE TRANSPLANTED?

Organs that can be transplanted include kidneys, heart, lungs, liver, pancreas and small intestine. Tissues that can be donated include corneas, skin, heart valves, bones, veins, cartilage, tendons and ligaments which can be used to restore sight, cover burns, repair hearts and mend damaged connective tissue.

The slogan of the South African Organ Donor Foundation is "one donor saves seven lives." In reality each organ donor can have an even greater impact than purely the people benefiting directly. Each transplant frees up places on dialysis programs and ICU beds for other patients.

BRAIN DEATH CERTIFICATION – WHAT IS CORRECT PROCEDURE?

Brain death certification is a standard of medical care. It must be performed rigorously and removes any and all doubt about prognosis. When brainstem reflexes are absent and there are no confounding factors the patient is 100% dead. It offers the family closure in a complicated situation where machines and medications are supporting organ systems.

Before commencing brain death testing ensure that:

1. The cause of brain death is specifiable and irreversible.
2. The effects of CNS depressing drugs and muscle relaxants have been excluded - 12 hours is the accepted norm in patients with preserved renal and liver function.

3. The rectal temperature is > 35°C and systolic BP is >90mmHg.
4. There is no endocrine or metabolic cause of coma.

Brainstem testing:

1. Pupillary reflex: Pupils should be fixed (unreactive to light) although not necessarily dilated.
2. Corneal reflex: No response to light touch with cotton wool. Don't damage the cornea.
3. Gag reflex: Absent on stimulating the back of the pharynx.
4. Cough reflex: No response to suctioning via endotracheal tube.
5. Pain response in facial distribution: Supra-orbital compression must not elicit any response in a facial distribution. Spinal and tendon reflexes may be present.
6. Oculo-cephalic reflex (Doll's eye movement): Ensure there is no cervical fracture. Lift the head to 30°. Turn the head to one side and open the patient's eyes. Keeping the eyes open turn the head rapidly through 180° to the opposite side. Any movement in relation to the head indicates an intact reflex. In the brain dead donor the eyes will stay fixed looking forward (like in a doll).
7. Oculo-vestibular reflex (Cold caloric test): Confirm the tympanic membrane is intact

and free from wax with an otoscope. Inject 20ml of iced water onto ear drum while holding the eyes open and look for any eye movements or nystagmus. In a brain dead patient there won't be any movement.

8. Apnoea test (Done last):
Ventilate the patient fully on 100% oxygen for 10 minutes. Do an arterial blood gas to check the $p\text{CO}_2$ is within normal limit (4.0 – 5.3kPa or 35 – 45 mmHg). Then disconnect the ventilator and place patient on a T-piece with O_2 flow rate of 15l/min. One of three things may take place:

- The patient may show some respiratory effort. The patient is not brain dead, although he may become brain dead at a later time. Replace on the ventilator. Consider for donation after circulatory death if decision is to withdraw support and death is expected.
- After 10 minutes there may be no signs of spontaneous respiration. A blood gas is done to confirm a raised $p\text{CO}_2$ of >6.6 kPa (50mmHg). In this setting the patient may be certified brain dead.
- The patient may desaturate or become haemodynamically unstable. Reconnect the ventilator but do a blood gas to see if the PCO_2 is adequately raised. If it is and there were no

spontaneous respirations then although the full 10 minutes is not up the patient may be certified brain dead.

- At the end of the test it is essential to reconnect the ventilator as breathing or not breathing through an ET tube unsupported hastens cardiac arrest.

An EEG is not required, nor is an atropine test, CT scan or angiogram. Legally the certification of brain death must be performed by two registered doctors independent of the transplant team, one of whom must have been registered for 5 years or more. The tests do not have to be done separately or within any specified time frame. The time of death is recorded as the time when the brainstem testing has been completed and is recorded as such in the paperwork.

REFERRAL PROCESS AND TAKING CONSENT

In South Africa we have an opt-in organ donation policy. There is no presumed consent and the family is asked to consent to the donation of the organs. Obtaining consent is often difficult in the grieving family and is a highly specialized field best performed by the transplant co-ordinator who has time to deal with the family and is intimately familiar with the transplant process. (How long does the transplant take? What will be taken? How is the body to be released to the family? Who will the organs be given to? What incentives are there to donate the organs?) Correct protocol is for the treating doctor to explain the clinical situation clearly and unambiguously to the family and to allow the transplant co-ordinator to take the discussion further.

Inappropriate choice of words or lack of clarity can be the difference between successful donation and refusal by the family. Families will cling to any scrap of hope and merely by saying the ventilator is all that is keeping the patient "going" can imply life to a desperate family. To stress again, it is important for the treating clinician to be very clear about the prognosis of the patient (there is none) and to call in the transplant co-ordinator early so that there can be every chance of obtaining consent from the family.

Absolutely no incentives are allowed to be used in obtaining consent. Financial or otherwise. Ethically it would start a slippery slope which is best avoided completely. No assistance with the funeral costs is possible. There is no prioritizing of another family member who may be awaiting a transplant. Donation is an altruistic event. The donation is not publicized to prevent unwanted contact between the donor family and recipient. Recipients often write a personal letter to the family thanking them and the transplant co-ordinator follows up with all families to check that they are satisfied with the process.

In Spain there is presumed consent and all end of life cases are considered potential donors by default. This combines with an excellent transplant co-ordinator program and a very active donation after circulatory death program to result in one of the highest organ donation rates in the world. In South Africa we rely on clinicians to refer patients. Spain has a donation rate of 38 pmp (per million population) compared to the 2 pmp of South Africa.

RELIGIOUS CONSIDERATIONS

Donation of a family members' organs is a very personal decision and numerous factors come into play such as education, socio-economic status and religious beliefs. There is however

no culture or religion on earth that prohibits the principle of giving or of preserving life.

The most important aspect is open communication that allows the entire process to be as transparent as possible, allowing trust to develop between the medical teams and the family. Wishes must be respected and no unnecessary duress added. Forcing the issue is counter-productive and the counseling process is best handled by someone well versed in all the possible situations. Merely asking does not add undue pressure and actually helps families to come to terms with the death.

Although deceased donation was initially not practiced in most Muslim countries. It is now routine throughout the Muslim world with most countries having started with living related donation. Once the obvious benefits of transplantation became apparent, and with religious leaders support, these countries have expanded into deceased donation in order to meet the need for organs.

LEGAL REQUIREMENTS

Consent is required from the next of kin – spouse, parent, brother, sister, or child (providing they are over 21 years of age) or legal guardian. Make sure to record all the contact details of the next of kin. If the cause of death is unnatural and therefore requiring a post-mortem - consent is needed from state pathologist/district surgeon. Consent is also needed from the medical superintendent/hospital manager at the hospital where the donor operation is to be done.

In the absence of family the medical superintendent/state pathologist is able to consent for organ donation but in practice this is not done. Therefore every attempt must be made to contact family members in order to allow consent to be obtained. The transplant co-ordinator has all the

appropriate documents and will obtain all the consents.

MANAGEMENT OF THE DONOR

The best place for the organs while all logistics are being sorted out is within a well-functioning body. Therefore the brain dead donor is fully ventilated to maintain a saturation of $> 90\%$ ($\text{PaO}_2 > 12 \text{ kPa}$). Body temperature is kept $> 35^\circ\text{C}$. The blood pressure is maintained with a systolic BP $> 90\text{mmHg}$. Two reliable IV lines are required (preferably one central line) as fluid resuscitation is often ongoing. If inotropes are required a dopamine infusion at $3\text{-}5 \mu\text{g/kg/min}$ titrated to the BP can be used.

A catheter is essential to monitor urine output which is targeted at 100ml/hr . Donors may become polyuric (secondary to the brain injury and ADH secretion) and require large volumes of fluid to maintain adequate urine output (can even be > 1 liter per hour). Check arterial blood gases, serum electrolytes, urea, creatinine and glucose regularly and correct when necessary.

Once consent is obtained for donation management of the donor becomes the responsibility of the transplant team. The transplant coordinator is an ICU trained nurse and will manage the patient up until the donor operation. This helps minimize the disruption to clinical services and not divert staff away from their existing clinical duties.

In China there is concern over the use of organs from executed prisoners. Due to this ethical concern no publications from China are published in the international literature and speakers are not invited to international conferences.

DONOR OPERATION

The brain dead donor is taken to theatre, cleaned and draped for a full sternotomy and laparotomy. The

cardiac team and the solid organ team work concurrently to isolate the great vessels throughout the body. Once proximal and distal control is obtained in both the chest and the abdomen cannulas are placed in the aorta allowing for in-situ cold perfusion of the organs. When everything is ready the ventilator is switched off and up to 12 liters of ice cold preservation solution is run in. The body cavities are also filled with ice cold saline to help rapidly cool the body. The organs will become pale as all the blood is flushed out - vented from an IVC incision into the chest cavity. Once adequately flushed the organs are dissected out. First the heart, then the liver and lastly the kidneys. The organs are triple bagged, suspended in preservation solution and placed on ice. The eye and skin teams have up to 24 hours to procure their organs. The eyelids are closed afterwards and skin is only taken once the body has been turned enabling less traumatic viewing by the family.

TIME-FRAMES – WHAT IS THE RUSH?

All organs function better and last longer the sooner they are transplanted and reperfused in a recipient. Heart transplants have a limit of 2 hours of cold ischaemic time, a liver 12 hours and kidneys up to 24 hours.

ALLOCATION PROCESS – HOW IS IT FAIR?

In South Africa organs are allocated within each province. This helps to limit cold ischaemic time. Recipients must be an ABO blood group match to receive a solid organ. The recipients have blood taken every 3 months which is kept at the tissue typing laboratory - this is used to screen for preformed antibodies as their presence would preclude transplantation. The recipients are selected based on a combination of how good the match is and how long

they have been waiting for a transplant. Race and socio-economic status do not come into the equation. In South Africa the average waiting time on dialysis before transplantation is 5 – 6 years. The mortality rate while waiting for a kidney transplant is 5% per year and a further 2% of patients will become too ill to transplant. The waiting list for heart and liver transplantation is much shorter as these patients die while waiting due to the lack of a method of long term organ support. Donors for these organs also need to be matched for height and weight. If there is no ideal recipient locally (within the province) the organs are allocated nationally.

The Declaration of Istanbul provides ethical guidelines regarding the practice of organ donation and transplantation. It states that organ trafficking and transplant tourism should be prohibited because they violate the principles of equity, justice and respect for human dignity.

Recipient Operations

Heart and liver transplants require the removal of the existing organ prior to replacement. A cardiac transplant recipient is placed on bypass prior to removal of the heart and the heart is anastomosed directly in place of the old heart - donors and recipients are size matched.

The liver is unique in that it has the ability to regenerate and hence can be altered in size during back table preparation to fit a child or split to supply two recipients (usually a child and an adult). First the new liver is connected to the IVC and portal vein. The liver is then reperfused - it gets 70% of its blood supply from the portal vein. The hepatic artery is next followed by the bile duct which is anastomosed to the remnant bile duct or to the bowel with a hepatico-jejunostomy.

Kidneys are transplanted in the extra-peritoneal space onto the external iliac vessels. An oblique incision is made

from just above the iliac crest to the symphysis pubis. This position is easy to access, provides good exposure of the vessels and is close to the bladder for the ureteric anastomosis. The vein is done before the artery and the kidney is reperfused prior to connecting the transplanted ureter onto the bladder.

Post-operative stay varies but patients require very close monitoring of their fluid status and may need temporary organ support in the ICU to help them recover. They were until quite recently dying. Initially very strong immunosuppression is given to prevent acute rejection but this places patients at increased risk of infection. Immunosuppression is lifelong but is tapered over time to balance the risk of rejection and against infection.

In Pittsburgh, a major pioneering centre in transplantation, the operation would be done the same way every time in order to standardize it and allow Professor Thomas Starzl (famous for the first liver transplant) to walk into theatre at any stage and know immediately what had been done and what still needed to be done.

LIVING DONATION

Donating a kidney carries a mortality risk of 0.03% and is widely practiced. Living donor liver transplants are also performed but the risk to the donor is more substantial, carrying a mortality of 0.6% and a morbidity of 10%. Living related liver donation is possible because the liver is the only organ with the ability to regenerate and 30% of a good liver is enough to prevent acute liver failure.

Living donors are extensively investigated to ensure that all risks are minimized and that the transplant will have every chance of success. Initial workup entails determining that the blood group is a match and screening for factors that would preclude donation. Criteria are stringent as

these patients are unique in medicine, in that they do not have any indication for the surgery themselves. Any co-morbid disease, end organ damage or lifestyle that may put the potential donor at future risk of organ failure would result in them being turned away and referred to the appropriate medical team. The work-up includes a full social and psychological assessment. In cases where multiple donors come forward the lowest risk patient with the best HLA match is used.

In Iran there is a formal system of paid living unrelated donation. This is the only country with such a system. Other countries do not practice this due to ethical concerns regarding perverse incentives and that the net flow of organs will be from poor to rich. In South Africa all living unrelated transplants have to be approved by the Minister of Health. e.g. Husband donating to wife. There is evidence to support that transplants between emotionally linked individuals have a better long term outcome than cases where there is no link.

SUMMARY

Organ donation in South Africa depends on you the treating clinician to continually be on the lookout for potential donors. The correct process needs to be followed in terms of brain death testing and an early referral to the transplant co-ordinator allows the best chance of consent.

The number of potential donors has been expanded by using *extended criteria donors* and the possibility of *donation after circulatory arrest*. It is important to be aware of this and to refer early in cases where there is planned withdrawal of support and death is expected to occur rapidly. The transplant team is responsible for managing the donor and will arrange all logistics.

Thank you for helping to turn the loss of a patient into an opportunity for new life in others. Not an easy thing.

FAMOUS ORGAN TRANSPLANTS - WITHOUT THE UNSUNG DONORS, DOCTORS AND NURSES THE FOLLOWING WOULD NOT BE POSSIBLE...

Jonah Lomu – New Zealand rugby player – received a living unrelated kidney transplant in 2003 for nephrotic syndrome. The kidney was transplanted in a deeper position than normal to allow him to play contact sports.

Dick Cheney – US Vice president under George Bush – received a heart transplant in 2012 for ischaemic cardiomyopathy having been on waiting list for 20 months. He had previously had 5 heart attacks related to his 60 pack year history.

Evil Knievel – motorcycle stunt rider – contracted Hepatitis C from a contaminated blood transfusion. He received a liver transplant in 1999 but died from idiopathic pulmonary fibrosis in 2005

Manto Tshabalala Msimang – South African Health Minister - received a liver transplant for autoimmune hepatitis in 2007 but succumbed to complications related to the transplant in 2009.

Eric Abidal – Barcelona football player – underwent a living related liver transplant from his cousin in 2012. He returned to play for Barcelona but was traded to Monaco in 2013.

Chris Klug – Olympic snowboarding bronze medalist – received a liver transplant in 2000 for primary sclerosing cholangitis. He won his medal after his transplant.

Steve Jobs – Apple founder and CEO – underwent a liver transplant in 2009 for metastatic neuroendocrine tumour

of the pancreas. He died in 2011 from metastases to his lungs.

Linda Lovelace – actress in the movie Deep Throat – received a liver transplant in 1987 for Hepatitis C related cirrhosis. She died in a car crash 15 years later.

Alonzo Mourning – Miami Heat basketball player – developed renal failure from focal segmental glomerulosclerosis and received a kidney transplant in 2003. He won the NBA championship in 2005 with the Miami Heat and Shaquille O’Neal.

Sarah Hyland – actress Modern Family – born with renal aplasia received a kidney transplant from her father in 2012 when her renal function had deteriorated to a point approaching dialysis.

Tracy Morgan – actor from 30 Rock – underwent a kidney transplant in 2010 for diabetes associated renal failure.

South Africa currently has a waiting list of 5000 patients awaiting transplantation and we have a deceased donation rate of 2 per million of the population. South Africa performs an average of 320 transplants per year.

HOW DO YOU REGISTER TO BE AN ORGAN DONOR?

www.odf.org.za

0800 22 66 11

info@organdonor.org.za

<https://www.facebook.com/organdonorfan>

FORWARD - HOW CAN YOU DO MORE TO HELP ORGAN DONATION?

Take every opportunity to discuss and educate fellow professionals and the public correctly about organ donation. Aside from just registering with the organ donor foundation (ODF) family

and friends need to be informed of your decision.

Stay informed and active. Transplantation is a rapidly evolving field but it is the shortage of donor organs and misinformed people which are the biggest obstacles to saving lives with transplantation.

Stay alert to any opportunity for organ donation and always consult rather than not. The effort is always appreciated.



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