



Transplant News

Vol 16 No 3 Issue 59 - September 2017

Official newsletter of the
South African Transplant Society

50th Anniversary of the 1st Human Heart Transplant - SPECIAL EDITION

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Editorial

Professor Jerome Loveland
Editor

What a memorable edition of Transplant News this is, published to coincide with the 27th Congress of the South African Transplantation Society, which is commemorating the 50th anniversary of the world's first heart transplant! This took place in Cape Town in 1967, and as South Africans we can be truly proud to be associated with such a rich history of transplantation.

The lead article in this edition, elegantly written by Johan Brink, Tim Pannel and Karen Seele gives a wonderful overview of this first cardiac transplant procedure, but poignantly emphasises the ethical dilemmas and the impact of definitions and decisions around brain death which the team faced at the time. Whilst donation of organs after brain death has a massive impact on the rates of transplantation in South Africa and certainly worldwide, this is particularly pertinent for cardiac transplantation. Where both liver and kidney transplantation are possible using living donor organs, this is not the case in heart

transplantation, where living donation is not feasible for obvious reasons. Thus, relying on organs from deceased donors, it is as ever the responsibility of the entire transplant community to continually advocate for donation of organs after brain death. Through organisations like SATS and the ODF, particularly working in collaboration, an enormous amount of work is being done, and progress being made. However, we remain well short of the benchmark set by world leaders in the field.

Whilst many of the actual transplant operations have remained the same for many years, aside from relatively minor technical variations, massive developments have been made in the field of immunosuppression, and it is these advances that have made solid organ transplantation sustainable in the long term. Work continues to develop transplant models based on stem cells and basic structural lattices, ultimately obviating the need for a human organ but it is the progress in refining our immunosuppression agents and regimens that allows us to continue transplanting these organs that our patients so richly deserve.



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ZA1708684061

Heart transplantation

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Almost 50 years ago, on 3rd December 1967, the world's first human to human heart transplant was performed by Dr Christiaan Barnard at Groote Schuur Hospital. This was, and probably will remain, the most publicised medical event of all-time, headlining nearly every international newspaper, magazine and tabloid within days of the transplant. The idea of transplanting a heart from one human to another captured the minds and imaginations of the public like no other medical event before or since. The only other iconic event in that era which was equally well-publicised was man's first landing on the moon 18 months later.

Brain-dead donor - an emotional debate

This first heart transplant placed Groote Schuur Hospital, the University of Cape Town and South Africa firmly on the international medical map. A heart transplant was seen by the public as transplanting the very soul of an individual from one person into another and provoked tremendous debate, some very emotional, around the ethics of transplantation and spurred on the International medical and philosophy community to develop the concept of brain death into law. Many countries around the world took many decades to adopt laws - most notably Japan, which took another thirty years (until 1997) to allow organ transplantation from brain dead donors. Japan's first heart transplantation in 1968 led to the arrest of the surgeon who was charged with the murder of the donor, and similar incidents occurred around the world in the decade following the first transplant until brain death was more widely accepted. Even today many countries do not accept brain death, preventing organ transplantation as a therapeutic option.

Immunosuppression - the biggest challenge

This tremendous publicity generated by the first heart transplant occurred despite kidney and liver transplantation having preceded heart transplantation by many years. These prior surgical innovations were instrumental in paving the way for immunosuppression, vital for modifying the recipient immune response and preventing rejection from a genetically non-identical donor. The suppression of host-rejection as well as the prevention and treatment of subsequent side-effects remains the biggest challenge in organ transplantation.

Length and quality of life - the ultimate goal

Ultimately, the goal of a heart transplant is to improve both the length and quality of life and is indicated when medication and conventional cardiac surgery will not adequately alleviate symptoms of heart failure. As far as possible transplant teams

strive to help a recipient lead a life as similar in quality to that of his or her peers, unconstrained by the limitations of heart failure. Although transplantation remains a successful procedure for the vast majority of patients, the ongoing care of heart transplant recipients is a challenge and requires intense follow-up by the transplant team and diligent compliance by the patient.

Technical variations

The operation itself has changed very little since Dr Shumway from Stanford University in the USA, first described the technique in animals in the early 1960's. Small technical variations, the use of heart preservation solutions, as well as the improvement in the heart-lung machine have optimised this procedure through the decades. The lack of donors has also been offset by the use of implantable assist devices (miniature mechanical pumps that help the heart) as a bridge to transplantation as well as the recent use of donors whose hearts have stopped (donation after circulatory death, DCD), which would have been previously deemed unsuitable for transplantation. DCD hearts require resuscitative equipment and infrastructure that is not presently available in South Africa and assist devices are currently only accessible to patients with excellent health insurance.

Progress in post-operative care in the intensive care unit has made a significant improvement to early outcomes of heart transplantation, where patients without complications stay less than four days. In the last year Groote Schuur hospital instituted a long term extra-corporeal membrane oxygenation (ECMO) service, which brings the unit in-line with international standards for post-operative care in complicated cases. Once stabilised, patients are transferred to a general ward, where the post-transplant stay depends on the patient's general health and the function of the new heart. Age, general health, and response to the transplant all play a role in rehabilitation. However, most patients mobilise within a few days after surgery and are home within two weeks. Continued, regular outpatient follow-up and rehabilitation is essential for a good outcome.

New drug innovations

Approximately 15 years after the first heart transplant, in the early 1980's a "miracle" drug called Cyclosporin was discovered by Jean Borel, earning him a Nobel Prize. This drug was a significant breakthrough in the management of donor organ rejection and transformed transplantation from an experimental operation in leading academic medical centres to standard medical treatment for end-stage organ failure with reproduc-

ible results which could be applied more widely. The numbers of all organ transplants rapidly escalated in the early 1980's and reached a plateau a decade later when the availability of donor organs became the major constraint. Cyclosporin is within the class of drugs called Calcineurin inhibitors and the other commonly used drug within this class is Tacrolimus.

Calcineurin inhibitors are still the mainstay of treatment in organ transplantation, and its use has led to significantly fewer rejection episodes and a longer life expectancy. However, unwanted side-effects are a concern with this more effective immune-suppression. Higher incidences of infection, hypertension (high blood pressure), kidney damage and in some instances, long term kidney failure, diabetes, high cholesterol and cancers are some of the side effects of immunosuppression. Some of the newer immunosuppressive drugs show promise of a reduction of some of these side effects, although these remain an ongoing challenge in the period immediately post-transplant, as well as in the long term.

Psychological wellbeing

Over the years it became evident that psychological well-being is vital to successful outcomes in transplantation. In the first six months when steroid dosages are at their highest, feelings of anxiety, depression and in some extreme cases mania can develop. The importance of patient and family education as well as destigmatising these potential emotional problems is imperative. Carers have also learnt that patients who (for whatever reason), are unable to re-join work, have the potential to become despondent which may lead to depression. Those who are fortunate enough to return to work are sometimes regarded as chronically ill employees who take more time off work due to illness. Psychological and social support systems as well as treatment for depression need to be prioritised.

Major successes in the last 50 years

Following the significant milestone 50 years ago, the Christiaan Barnard Division of Cardiothoracic Surgery at the University of Cape Town have transplanted 537 hearts and remains the only heart transplant facility for state patients in South Africa, whilst also offering transplantation to private patients at UCT Private Academic Hospital. Despite the challenges that exist with heart transplantation, the outcome has improved significantly over the past twenty years. The functional status of the recipient after the procedure is generally excellent, depending upon the

individual's motivation, with an anticipated survival of 85% at one year, decreasing to 75% at five years.

The ongoing shortage of donor organs has fueled the search for alternative therapies for the failing heart. These therapies include mechanical artificial assist devices, which have been increasingly successful over the last few years - both as a bridge to heart transplantation and as so-called permanent destination therapy.



The Christiaan Barnard Division of Cardiothoracic Surgery at the University of Cape Town, are proud hosts of the international celebration to commemorate the 50th anniversary of the world's first heart transplant and give thanks to the donor families on the 2nd to the 4th of December 2017 at Groote Schuur Hospital.

Assist devices and Xeno-transplantation

The cost of these devices with an initial outlay of over R2 million, and ongoing maintenance of a few hundred thousand Rand annually (and with the occasional need for replacement of the devices), places this outside the reach of the vast majority of South Africans. However, a few fortunate South Africans have had the financial resources available to pay for these devices in the private sector.

The holy grail of organ transplantation will remain the development of genetically engineered animals to provide organs compatible with the immune system of humans (Xenotransplantation). Much research in this field has taken place over the last 20 to 30 years and although various immunological barriers have

been overcome, and genetic breakthroughs have been made to the point that organs from genetically discordant animal species have been successfully transplanted into primates, there is still a long way to go before Xenotransplantation becomes a clinical reality for humans with organ failure.

International Commemoration (2-4 December 2017)

The Christiaan Barnard Division of Cardiothoracic Surgery at the University of Cape Town, are proud hosts of the international celebration to commemorate the 50th anniversary of the world's first heart transplant and give thanks to the donor families on the 2nd to the 4th of December 2017 at Groote Schuur Hospital. Details will follow in the media in the next few months. We hope that the celebration of this courageous and innovative event will not only ensure the long-term treatment of heart failure patients but inspire young academics to follow in the legacy of Christiaan Barnard and his team five decades later.

Happy healthy heart transplant

Abby Courtenay
Registered Dietician
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Sandton



Whether you are awaiting a heart transplant, or recently went through the procedure, nutrition is vital every step of the way. Here we will discuss optimal nutrition goals before your transplant, directly after and in the long-term.

Nutrition before your transplant

Before your heart transplant, a dietitian will assess you and advise the following lifestyle changes:

Lose weight if necessary

Your BMI at the time of your transplant is an important predictor of your post-transplant outcomes. Body Mass Index (BMI) is the most widely used parameter to characterise differences in body weight.¹ If you fall within the extreme BMI classifications (underweight or obesity), you are at a much higher risk of infection and organ rejection.² Here are the BMI classifications endorsed by the National Institute of Health and the WHO:¹

BMI classifications endorsed by the National Institute of Health and the WHO ¹	
BMI	Classification
<18.5kg/m ²	Underweight
18.5 – 24.99	Normal
25 – 29.99	Overweight
30 – 34.99	Obesity class 1
35 – 39.99	Obesity class 2
>40	Obesity class 3

It is difficult to lose weight on your own, as the types of food, quantities and timing of your meals all needs to be considered. Use the guidelines below to optimise your diet and consider contacting a dietitian to assist you with an individualised eating plan to help you lose weight.

Optimise your diet and manage chronic diseases (like high blood pressure, high cholesterol and diabetes).

Ensure you are getting a balance of macro and micro nutrients

A balanced diet results in a balanced intake of all the nutrients you need to be healthy. If you are malnourished (over or under), your risk of infection after your transplant increases substantially.¹ A Mediterranean style diet is a protective way of eating that could help manage chronic diseases and prevent new ones from developing.^{1,2}

Focus on whole or minimally processed foods, limit red meat and alcohol and avoid fast foods, sugar sweetened beverages, refined grain products and processed/energy dense foods:²

• **Plenty vegetables, salads and vegetable soups**

Vegetables are low in calories, but high in vitamins, minerals, phytonutrients and fibre. This makes them ideal for those who want to enhance their health whilst maintaining or losing weight.²

• **Healthy unrefined starches** like legumes (beans, lentils, chickpeas) quinoa, barley, bulgur wheat and corn or high fibre starches like seed/ rye bread and high fibre crackers.²

Unrefined starches are less likely to cause spikes in your blood sugars (leading to improved energy levels and weight loss). They are high in fibre, which keeps you feeling fuller for longer (reducing the desire to overeat) and significantly reduces your risk for heart disease and stroke.²

• **Lean proteins** like fish, skinless chicken, lean beef or lamb, eggs or low fat dairy and healthy plant fats like olives, olive oils, avo, nuts and seeds.

Lean proteins are low in saturated fats. When saturated fats in the diet are replaced with plant fats, there is a reduction of heart disease. This benefit is not seen if saturated fats are replaced with refined carbohydrates.² Ask your dietitian how much protein you should be having every day, if you have problems with your kidneys, she may advise a low protein diet.¹

Eat a low salt diet²

- Avoid sprinkling salt onto your food.
- Avoid processed foods like polony and salty snacks like chips.
- Use stock cubes, soup powders and Aromat sparingly.
- Rather cook with herbs and spices (curry, masala, turmeric, pepper etc) or lemon, onions, garlic, chillies and mustard.

Start exercising²

Restrict alcohol intake and stop smoking.

Nutrition directly post-transplant²

Your dietitian will alter your diet to ensure the following:

- That you have enough energy and protein to promote wound healing
- Ensure that your electrolytes (sodium, potassium and chloride) are balanced
- Ensure optimal blood sugar control



Optimise your diet and manage chronic diseases (like high blood pressure, high cholesterol and diabetes).

You will initially be placed on a clear liquid diet and will then progress to a soft diet. Supplements or high calorie foods may be used to meet your increased needs or if you have a poor appetite.²

Nutrition for long term heart health

The aim of nutrition post-transplant is the following:

Prevent infection by following strict food hygiene¹

- Do not eat any raw foods for 6 months following your heart transplant (that means no sushi!).
- Mixed meals (such as casseroles), should be cooked and eaten immediately. If this is not possible, they should be covered and refrigerated and consumed within 24 hours.
- No raw foods should be added to cooked foods and then consumed.
- Wherever possible, keep sauces separate from cooked foods to prevent spoilage.

Prevent excessive weight gain and control high blood pressure and cholesterol²

On average, most recipients gain up to 10kg post-transplant. This excessive weight gain increases your risk for secondary chronic diseases. These secondary diseases then in turn increase your risk for new heart attacks.¹ This weight gain can be attributed to poor eating habits, decreased physical activity and immunosuppressive drugs (used to prevent your body from rejecting your new heart).¹ The good news is that you have control of 2 of these 3 risk factors, diet and exercise. In addition to this, consider talking to your dietitian about including stanols and sterols in your diet to help lower your cholesterol.²

Minimise osteoporosis risk^{1,2}

Post-transplant osteoporosis occurs frequently in heart transplant patients with most of the bone loss occurring after the first 3 months - 2 years. For this reason, it is vital that you optimise your bone density prior to your surgery. Before and after your surgery, you should aim to do weight bearing and muscle strengthening exercises to reduce your risk of falls, fractures and to increase your bone density.¹ Make sure you have an adequate intake of calcium. Calcium foods include low fat dairy (milk, yogurt or cheese), tinned fish (like canned salmon, sardine's and pilchards) and fortified foods like soya milk and tofu. If you are unable to meet your recommendations through your diet, ask your dietitian about calcium and vitamin D supplementation.

Conclusion

Whilst this information can guide you towards better health pre and post-transplant, it would be wise to visits a dietitian so she/he can assess your current lifestyle and help you make the necessary changes. Find a dietitian by visiting www.adsa.org.za

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Exercise and the heart transplant patient

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Many people are affected by different diseases of the heart, which affect the heart's functioning. An umbrella term for such disorders that affect the heart is "congestive heart failure". This is when the heart is unable to efficiently pump blood to the body, meeting all the body's needs.

There are many different causes of heart failure, some of which include coronary artery disease, high blood pressure, valvular dysfunction, atrial fibrillation and previous myocardial infarction (heart attack). A hereditary genetic disease with which one is born may also result in heart failure.

As the severity of the heart failure increases, exercise tolerance drastically declines, with most people suffering from dyspnea (shortness of breath), edema in the lower extremities (swelling/water retention in the legs) and excessive tiredness. As a result of the inefficient heart, most sufferers become more sedentary, leading to a host of further complications.

It is important to try and continue being physically active, despite cardiac dysfunction. Exercise for persons with heart failure should be closely monitored by a health professional (biokineticist) under the guidelines of a cardiologist who has performed a stress ECG to determine limits for exercise safety. Exercise must be closely monitored and should incorporate cardio-respiratory training as well as muscle strength and endurance training.

The first successful heart transplant was performed by Dr. Christiaan Barnard in 1967. Heart transplants have become an increasingly utilised and accepted treatment for those suffering with heart failure. There are, however, a few criteria which need to be met in order to undergo heart transplantation, some of which are:

- Severity of the disease
- Body conditioning (one needs to be within a healthy BMI range)
- Muscle mass
- Age requirements
- Mentally and psychologically fit for transplant.

Prior to transplant, one needs to be physically fit as the surgery takes a major toll on the body. One often loses a substantial amount of weight while recovering in ICU. It is therefore advisable to try and maintain some form of exercise while awaiting transplant, to avoid pre-transplant deconditioning.

Once one has received a heart transplant, it is important to try to mobilise as soon as possible, to limit muscle atrophy (losing muscle mass), and to decrease stress on the body.

Following a heart transplant, the newly implanted heart is denervated. This occurs when both the sympathetic and parasympathetic nervous systems are not "in sync" and functioning optimally with the newly transplanted heart. It is important to note that this denervation leads to an abnormal heart rate response to exercise and one's exercise capacity.

One's resting heart rate is usually above the normal range, and it is often found that one's heart rate does not respond normally (as in the healthy population) to increased exercise. A transplanted heart struggles to reach upper boundaries of maximum heart rate response. It also takes a longer period of time to return to resting heart rate. It is common that post heart transplant patients are placed on medication to control their heart rate such as beta-blockers and/or calcium channel blockers. In some instances patients may also require a pacemaker to be inserted to control heart rate response.

Research has shown that in some cases, exercise can assist with normalisation of autonomic control of the heart. Reinnervation occurs in 40% - 70% of people in later stages post heart transplant. (The heart is able to respond more normally to hormones such as adrenalin, that controls heart rate).

Exercise is an integral part of recovery from a heart transplant. From a very early stage, a physiotherapist will assist you to mobilise out of bed and get back on your feet.

Some form of exercise should be done daily, with both cardio respiratory training as well as strength training in mind. There are however a few precautions that need to be adhered to:

- During transplant, the sternum is often dissected and bone takes approximately 6 weeks to heal. One should not perform any upper-body weight training during this period in order for the bone to properly graft and recover. After approximately 6 weeks, and when the doctor is happy with incision-site healing, one can slowly incorporate upper extremity range of motion and light resistance training.
- Heart rate should not be used to determine training zones. As previously discussed the heart is denervated, thus a typical heart rate response is seldom observed. A better measure of intensity that should be used is the Borg scale of physical exertion or rate of perceived exertion (RPE). A level between 12-14 on this scale should be used (somewhat difficult).
- Research shows that exercise capacity post-transplant is reduced, as a result of many different factors including: Sympathetic nervous system response (hormones controlling heart rate), previous deconditioning, resting heart rate and

- drugs taken post-transplant (anti-rejection, cortisone).
- Exercise should include both aerobic as well as resistance training, and should be performed in 45-60 minute bouts, approximately 3-4 days per week.

Exercise can remarkably prevent complications following heart transplant such as reducing blood pressure, renal failure, diabetes and graft failure. Exercise also improves healthy weight gain, exercise capacity, muscle strength and psychological well-being.

References available on request.

My transplant journey - 21 years with my “new” heart

Kasandra de Kock
Heart transplant recipient



We interviewed a 31 year old heart transplant recipient who was born with a defective heart that was enlarged, had the four chambers switched around and a leaky valve.

Likes, hobbies and interests: Arts and crafts, watching movies, reading/research, baking and spending as much time with my little son. I love baby kisses and hugs, funny people and waking up positive in the morning.

Dislikes: I loathe global warming, hospitals, rudeness, dishonesty and negative, toxic people.

When and where did you have a heart transplant?

30 October 1996, Red Cross Children’s hospital in Cape town

How has having a transplant changed your life?

Being a heart transplant survivor, I can say that what really changes is a person’s perspective on life. We literally go from death’s door to healthy and in doing so, we tend to have a keener appreciation for what being alive means and what life is about.

What are the challenges of your lifestyle as a transplant patient?

I need to take lifetime immunosuppressant medications to prevent rejection and other medications to control their side effects. I need to have regular check ups and follow a healthy diet and exercise regularly.

What resources have helped you cope?

Research websites, the story of Derek Fitzgerald is my inspiration – he is my role model.

What advice would you give to people contemplating having a transplant?

The most important thing to keep in mind is that you, the

potential recipient, must take ownership of the process. As the person with the most at stake, you are ultimately responsible for getting things done. If you are unable to do this yourself, it is imperative that you get a loved one to act on your behalf.

Advice to new transplant recipients:

- be thankful for your second chance
- take your necessary medication
- follow a healthy diet with a good exercise plan
- have regular check ups with your doctor
- don’t take any risks that will affect your health and which you will regret later.

Anything else you would like to add?

In 2013 I discovered that I was expecting my first child. I informed the doctors once I did my first scan in July 2013. They weren’t happy about it, but I made a promise to myself that I would get through this pregnancy successfully. I followed a healthy diet as far possible and I attended cycling spinning classes everyday up until 7 and half months into my pregnancy.

Three years ago I became a very proud mommy of a beautiful healthy energetic blue-eyed boy. I am thankful for the second chance and I just want to thank my parents, siblings and friends for their love, great support and motivation. My son who continues to inspire and motivate me, plays a huge role in my life.

This year, on the 30th October 2017, I will have had my heart transplant for 21 years and I continue to get stronger everyday.

50th Anniversary of the world's first human heart transplant

Hennie Petrus Joubert
Heart of Cape Town Museum
Groote Schuur Hospital
Cape Town

The 3 December 2017 will be the 50th anniversary of the world's first heart transplant - a milestone in medical history.

Prof. Chris Barnard qualified with his MBChB at the University of Cape Town in 1946. He then went to the University of Minnesota in 1956 to study heart surgery with Prof. Owen Wangenstein. He was to complete a 6 year PhD which he completed in just 2 years, including a Master's Degree in Surgery. He returned to South Africa with a heart-lung bypass machine, given to him by the USA and a research grant of US\$2000 for three years.

On 2 December 1967, a 25 year old young woman, Denise Darvall and her mother were hit by a car not far from the hospital – the mother died on impact but the young woman was brought into the emergency room with extensive head injury – later a neurosurgeon declare her “brain-dead” with a flat-line EEG. Denise’s brave father, Edward Darvall, signed the consent form for her heart to be used in the heart operation as well as her kidney. The donor was taken to Operating

Theatre 1 where she was placed on a heart-lung bypass machine in order to keep the heart beating after it had stopped so that the heart muscle was constantly supplied with oxygenated blood. Prof. Barnard, in the meantime, was in operating theatre 2 preparing the recipient, Mr Louis Washkansky – a 54 year old patient who had suffered two previous heart attacks and was dying. The operation began once the anaesthetics had been administered at

1am on the morning of the 3 December. Prof. Barnard started the transplant at 2am and finally got the new donor heart beating at exactly 5:58 am – 3 hours and 58 minutes after starting the operation.



Prof. Christian Barnard prepares for surgery



Mr Louis Washkansky, first successful heart transplant recipient



Ms Denise Darvall, donor of the "most famous heart in history"



The world's first successful human heart transplant surgery made headlines all over the world

Mr Washkansky recovered very well and was pleasantly surprised at his easy breathing. He had a good appetite and joked with the nurses. Unfortunately, being a 40 cigarette a day smoker, his condition started deteriorating and the team decided that it could be rejection. He was given extra immunosuppressant but in actual fact, they later found out the problem

was pneumonia. At the autopsy, it was found that *Klebsiella* and *Pseudomonas* had invaded his lungs – having been made weak by the increase in immunosuppression drugs. He died after 18 days with the heart beating firmly until the end.

Visit the Heart of Cape Town Museum

Relive the historic medical surgery that changed and inspired world transplantation

Guided tours (7 days a week) start at:
09:00, 11:00, 13:00, 15:00

Specially pre-arranged tours are available for 17:00

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For more information, go to: www.heartofcapetown.co.za/

