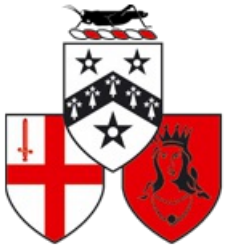

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The Artificial Heart: A New Ending? Transcript

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The Artificial Heart: a New Ending?

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"Hearts will never be practical until they can be made unbreakable."

The Wizard of Oz to The Tin Woodsman

Introduction

This talk covers the no man's land where plumbing meets ethics. It relates to what some have called 'the mother of all pump problems'; how to replace the amazing human heart. In my first Gresham Lecture as Professor of Physic in 2014 [1], I explained what the heart does and a little of how it works. To remind you, the human heart starts working within days of conception, and from then on works pretty well ceaselessly. It beats 100,000 times a day at rates which vary with the demand. 40 million times a year; 3 billion in an average lifespan. It distributes blood and nutrients through an estimated, but still astonishing, 97,000 km of blood vessels. And most of the time you don't even notice that it's there.

The rate at which the heart beats can range from as low as 40 in a very fit person at rest up to 200 beats per minute in peaks of exercise or stress (as we saw in our Formula One driver in a previous talk [2]). The amount of blood the heart can eject at each beat is called the stroke volume, and this can vary from 50 to 220 ml/beat, meaning that the cardiac output, which is the product of heart rate and stroke volume (expressed in litres/minute) can increase up to 5 or 6 times its resting level; sufficient to meet our most extreme needs. Power whenever you need it, and all mediated by a complex mix of nerve supply, hormones and feedback loops.

Sadly, this amazing organ can fail, either from congenital and genetic problems such as inherited heart muscle disease (cardiomyopathy) or secondary to congenital rhythm problems; or from acquired disease such as viral infections, coronary artery disease, high blood pressure, drug damage or secondary to abnormal rhythms. Whilst you can have a severe cardiomyopathy characterised by very thick muscle obliterating the heart cavity, it is dilatation of the heart muscle that is more common; this variant is known as dilated cardiomyopathy. In this condition the affected ventricle of the heart resembles an over-inflated balloon, and contraction is reduced, limiting the amount of blood ejected each beat (stroke volume) and hence cardiac output. This dilated ventricle eventually reaches a situation in which basic mechanics accentuate a vicious circle. As the heart fails, the diameter of the heart increases and so does the wall tension (following the Law of Laplace [see Gjesdal (2011) [1] for a detailed explanation]), which both restricts blood flow (as capillaries get stretched and compressed) and increases oxygen consumption. Not good, and progressively fatal without treatment. These changes can now be observed and measured in some detail using non-invasive imaging echocardiography and MRI techniques.

The consequences of heart failure are severe. Firstly, effective distribution of necessary resources is severely hampered; peripheral organs do not get the oxygen and food they need to function satisfactorily, especially during exercise or other stresses. Secondly, pure hydraulic forces come into play. The inability to pump blood forward effectively means that there are upstream problems associated with the higher venous pressure, developing as it becomes increasingly heard to fill the dilated and stiff heart. This higher venous pressure forces fluid to leak out of blood vessels into the tissues. In the lungs, this causes pulmonary oedema, which my grandmother used to call 'water on the lungs'. In the peripheral tissues, and especially the ankles and abdomen, water accumulates to create swollen ankles (with pitting oedema, a 'pit' appearing and remaining for a while after a finger is pressed into the affected area) or ascites (excess fluid in the abdominal cavity). Affected people become exhausted on even minimal effort, and appetite and quality of life rapidly deteriorate. Eventually they need hospitalisation or palliative care.

Heart failure represents, as Veronique Roger points out [2], "*a staggering clinical and public health problem".* In the United States in 2013, 5.8 million people were being treated for heart failure, with currently over 650,000 new cases being diagnosed each year. About 1 in 5 of us will develop heart failure in the course of our lives. It has been estimated that, worldwide, about 25 million people are living with heart failure. It is not a benign disease. There is significant mortality (only 50% survive for 5 years and less than 10% survive 10 years) and morbidity and, of course, a resultant huge cost both to the individual and society. This cost is not related to an increased incidence of the disease, but rather to the chronic nature of the problem, the drug and other treatments, and repeated hospitalisations.

The Management of Chronic Heart Failure

One might describe the management of CHF as passing through several phases, **from help, through repair to support and finally replacement.** The severity of heart failure is itself divided into stages, with Stage D being the most advanced. A variety of drugs are used to help in the early stages of the disease, all aimed at

treating underlying conditions, such as high blood pressure, or reducing the work of the heart. Most treatment is aimed at slowing the inevitable advance of the disease, and there are excellent published guidelines for its management; **https://www.heart.org/idc/groups/heart-public/@wcm/@hcm/@gwtg/documents/downloadable/ucm_456868.pdf** from the American Heart Association and **https://www.nice.org.uk/guidance/cg108** from NICE in the UK.

Several **surgical approaches** have been tried over the years[3]. Some very innovative attempts failed to fulfil their promise and have been abandoned. These include using the large muscle of the back (latissimus dorsi) to wrap around the heart in an attempt to use it to share the load of contraction[4]. Over 1500 of these operations were done by Carpentier's Paris group, based on original ideas by Kantrowicz[5], but it proved relatively unsuccessful. Indeed, it was commented[6] "*that it appears that those who can survive the operation do not need it, and those who do need it cannot survive it".*

Other workers tried wrapping the dilated heart in an elastic net called a cardiac support device, to try and remodel the dilated shape of the heart and reduce wall stress. Although it slightly improved quality of life it, sadly it did not affect mortality [7]. A surgeon called Batista introduced[8] the concept of removing part of the left ventricular wall to remodel the heart and reduce wall stress. This too did not live up to expectations as the operative mortality was very high, as was the recurrence rate for heart failure[9].

Many groups have tried to use techniques of regenerative medicine, hoping to induce either new heart muscle cell growth or remodel existing cells, by employing stem cells. This is a complex and relatively new field, and as yet there are no really effective solutions emerging [10].

In some patients, the cardiac changes result in abnormalities in the way the electronic signals causing the heart to contract are spread through the heart muscle. These abnormalities can accentuate the failure by rendering contraction uncoordinated, further lowering cardiac output. These patients can be helped by sophisticated electronic pacing of the heart, in so-called cardiac resynchronization therapy [11].

Conventional surgery of the heart is useful in selected patients. For example, those with established coronary artery disease may be helped by coronary artery grafting, although the exact benefit remains unclear [12]. Others are helped by repairing leaky valves or by removing locally dead, aneurysmal portions of the ventricular wall. These procedures, though, are really supportive rather than curative techniques.

Transplantation

The introduction of heart transplantation in the 1960's as a treatment for terminal heart failure brought new hope to patients with the disease. It remains a remarkable operation, and there is still some magic in watching a donor heart start and function well enough radically to improve the quality of someone's life. Sadly, such treatment is not available everywhere, and as I am sure you are aware, there are simply not enough donor hearts available to manage all the patients with heart failure who would benefit. The number of heart transplants being performed per year in the world has stayed remarkably static at around 3750 since the turn of the 21 st century, yet demand for organs is rising. There is a big gap between the low thousands of transplants and the millions of patients living with severe heart failure. What must it be like to be told you need a transplant, that you are eligible and a good candidate, only to discover that no donor is likely to come along, and you might die on a waiting list? The hopes of yourself and your family are cruelly dashed.

If you are lucky enough to get a heart, there is currently a median survival of around 11 years, although if you survive the first year after transplantation you can look forward to about 13 years of life. About 16% of patients are alive at 30 years post-transplant. These are still amazing figures, given that the indication for transplantation is predicted certain mortality. Patients need to be on a cocktail of anti-rejection drugs for life after transplantation. Although the quality of life is quite good in most cases, and the drugs have got better, many are toxic and not pleasant to take, and regular visits to hospital are needed to keep everything working well. Rejection, coronary artery disease and drug-related complications remain important adverse events.

Given the lack of opportunities for transplantation for most people, it is not surprising that scientists started to look for methods of mechanically supporting the circulation, or indeed replacing the heart with a man-made substitute.

Mechanical Methods of Supporting the Heart

I discussed in my second Gresham Lecture [3] the importance of the work of John and Mary Gibbon and their successors in developing the heart-lung machine which itself has led to advances in mechanical support for heart failure. Without their pioneering work none of what follows would have been possible.

Before going more deeply into some of the devices that have been invented in the last few decades, I want to tell you something about Paul Winchell, who died in 2005 aged 82 [4]. Winchell was a ventriloquist, who regularly appeared on TV in the US. Later, he went on to become more widely known as the voice of the wonderful Tigger in the Winnie the Pooh animations. He was invited for dinner at the home of Henry 'Hank" Heimlich, the surgeon who invented the Heimlich manoeuvre to treat choking due to a foreign body in the airway. They became friends

and Winchell asked to go and see heart surgery at Montefiore Hospital in New York where Heimlich worked. Sadly for Winchell, he found himself watching a surgeon called George Robinson lose a patient on the table, and it struck him that an artificial heart might have kept the patient alive. Heimlich told Winchell to use his puppet-making skills and go away and design an artificial heart. He did just that and, remarkably, filed a patent for such a device in 1956. There are striking resemblances between his design and those that have subsequently become successful.

Within the medical research community, much of the early development of the artificial heart was done in the animal laboratories of the Cleveland Clinic by **Willem Kolff** and his team[13]. Kolff is best remembered for inventing the artificial kidney, which has come to save the lives of thousands of people. **Dr Domingo Liotta** who worked with the Cleveland Clinic team moved to Baylor University in Houston in 1961, to work with two great pioneers of cardiac surgery, **Denton Cooley and Michael DeBakey,** and to develop further his ideas for the artificial heart. The principles behind the devices which have followed were beautifully presented in an early review article by Zuhdi et al[14], which outlines the extraordinary feats that an artificial heart must be able to perform if it is to work effectively in a human. Zuhdi et al calculated workloads, energy requirements and summarised potential designs, and described very early in the experience the potential methods of supporting the heart which might be used. He turned out to be correct.

Ever competitive academically and for operating space, Cooley left his partner to set up clinical practice at St Luke's Hospital and the Texas Children's Hospital and went on to found the Texas Heart Institute on the St Luke's site. However, he stayed on the academic staff at Baylor where the mechanical heart research program was thriving. Sadly for Liotta, the resources shepherded by DeBakey were concentrated on ventricular assist devices (which I shall discuss in more detail below) and after 8 years at Baylor, he decided to work with Cooley at the Texas Heart Institute. After Barnard's first heart transplant in 1967, Cooley rapidly became the surgeon in the world with the most transplant experience, and soon realised that there were not enough donors to meet the demand for transplants. Since Liotta was so frustrated by his experience at Baylor with DeBakey, he found a ready ear in Cooley.

Liotta thought that he had enough data to support the implantation of an artificial heart into a patient who would otherwise die on the operating table. Cooley had done rather well financially from his surgical endeavours, and decided to fund the research himself, getting the program off the ground much more quickly than by conventional routes. The two surgeons devised a system that would allow a four-chambered mechanical heart that would be driven by an external console. They worked with biomedical engineer William O'Bannan to devise the hydraulic mechanisms of the system. O'Bannan's used his own garage for the assembly of the drive console! After 15 years of Liotta's preparatory work, Cooley's funding allowed them not only to build a working heart in just 6 months, but also to implant it into 6 calves. The heart was constructed largely of biocompatible silicone and fabric material, and Cooley provided the valves to a design of his own, making the heart 40% more efficient than previous versions. The pumping mechanism itself was a diaphragm with blood on one side and CO_2 on the other, pulsed from a drive console, delivered by pipes to the synthetic heart. The device was not intended to be *permanent,* but to keep the patient alive long enough for a suitable donor heart to become available. This has become known as **bridging to transplantation.**

In March 1969, a 47-year-old patient from Illinois called Haskall Karp was admitted to St Luke's Hospital Houston suffering from terminal heart failure (and secondary kidney and liver damage) following a series of heart attacks. He was so ill he could not even brush his own hair, and was put up for a heart transplant. However, Cooley felt that his chances of getting a heart were minimal and so suggested that he have a ventriculoplasty (an operation to remove poorly contracting segments of ventricular muscle and to alter the shape of the heart and thus its dynamics), with a fall-back position of implanting the Liotta-Cooley artificial heart if the ventriculoplasty did not work. Karp, and his wife and with the support of their rabbi, signed consent for this very experimental operation, which went ahead on Good Friday, April 4 th, 1969. Cooley was far from sure there would be enough good heart muscle left after removing all the scar tissue from Karp's heart, but he went ahead anyway. Sure enough, Karp could not be separated from the support provided by the heart lung machine, and so it was decided to insert the artificial heart, which they had been testing in the calves.

Cooley removed Karp's dead heart, leaving a big space in the chest, and obviously no donor heart to insert. It must have been a remarkable moment for all those present. Liotta's artificial heart was brought to the table. The insertion was made easier by the design of the device, which allowed the left and right sides to be inserted individually to save space. Once connected to its console, the artificial heart began pumping and Karp could be weaned from the heart lung machine. Karp woke up and was weaned from artificial ventilation, and as Cooley said at the time, *"we were all relieved, and thought that the mechanical heart era had arrived".* Karp's wife made an emotional television appearance to announce to the world that he was being kept alive by such a machine, and everyone just hoped a donor heart would come along. Astonishingly, one did; just 64 hours after the insertion of the Liotta heart, Karp had it removed and a donor heart implanted. The donor heart appeared to be working well and everyone was very optimistic and thought a significant therapeutic milestone (mechanical bridging to successful transplant) had been passed. Sadly, and partially as a result of the anti-rejection therapy he had to receive, Karp developed severe pneumonia and worsening kidney failure. Just 34 hours after the transplant, Haskell Karp died.

Nonetheless, it had been demonstrated that the human circulation could be sustained for a long period with

mechanical support. Despite worldwide adulation for the effort, and for the device, Mike DeBakey was far from pleased. He was apparently unaware that Cooley was funding the project privately and thought the device 'inferior', although Cooley was quickly vindicated. It was the start of a media-driven rift between Cooley and DeBakey, which fascinated cardiac surgeons throughout the world, and which lasted until 2007. DeBakey, was a remarkable man, and amongst many achievements is credited with forming MASH units in the US army in the 2 nd World War, and in his late 80's he operated on Boris Yeltsin in 1996. DeBakey died in 2008, aged 99.

Meanwhile, over towards the west coast of the USA, a young man watched his father dying of severe heart disease, and became obsessed with idea of building an artificial heart. His name was **Robert Jarvik**. He was accepted to the University of Utah medical school and soon went into the lab run by Dr Willem Kolff, who had moved there from Cleveland. With his passion and energy, Jarvik had developed within 7 months an artificial heart that later became known as the Jarvik 7. The heart was also a compressed air driven membrane pump, which could be powered by a battery, although it was the size of a refrigerator! The FDA gave permission for implantation of the device, but only into patients who were otherwise certain to die. In 1982, a Seattle dentist called Dr Barney Clark (a 'tough old guy') was the first person to receive such a heart. Clark was in severe, near fatal, heart failure, and fully understood his condition; indeed he volunteered for the operation not expecting to live, but "in the interests of advancing science". Even Jarvik thought he would only live a few days. The implantation was successful, and the Jarvik heart worked well from a mechanical perspective, and those few days turned into months. Barney Clark lived for 112 days, but they were not happy days. He had constant infections, for which he received an array of antibiotics (probably causing pseudomembranous colitis), drifted in and out of consciousness, and suffered repeated blood clotting episodes and a series of strokes, the final one of which killed him. He had asked to be allowed to die on several occasions. It was a media circus, and there was a huge ethical debate about whether the approval processes had been appropriate. Pre-operatively, the Utah Institutional Review Board had defined a successful outcome as 'coming out of the operating room alive'. I suspect that would not have been accepted these days. However, within a decade, 236 of these Jarvik 7 artificial hearts had been implanted worldwide. The National Institutes of Health and the FDA in America had supported this research, rather with the enthusiasm of landing a man on the Moon. The New York Times in the late 1980's dubbed artificial-heart research "*a kind of "Dracula" that was sucking money away from more worthwhile programs*".

The Jarvik 7 continued to be developed and to improve in both the details of its engineering and the drug therapy used to support it. It morphed into a product called the SynCardia Artificial Heart, of which 1250 have been implanted giving over 350 patient-years of support. The longest a patient has been supported prior to a successful transplant with such a heart is 1,374 days [15]. The failure rate for the pumping diaphragm is less than 1%. However, the therapy is still regarded as a bridge to transplant, and the complication rates remain significant, with neurologic injury, bleeding, and infection being the most frequent[16]. Another model of artificial heart, using the same fundamental principles, emerged from the Texas Heart Institute experience. This was called the Abiomed total artificial heart. Results were similar, and still perceived as a bridge to transplantation.

There is a new kid on the block; the Carmat heart developed by Carpentier and his team [17] [18] in Paris with support from Astrium a spin off from the European Aeronautics, Space and Defence Company (EADS), which subsequently became Airbus. This is also a pneumatic heart, but with biologic valves and biocompatible surfaces. It has much more sophisticated and integral software that responds to the users exercise demands. It has so far only been inserted in 4 patients and more data are needed to know if it will be any good. It is hoped that the improved biocompatibility and greater rate and output variation will both reduce side effects and minimise the blood clotting and stroke complications which beset pulsatile devices.

There are other problems with these pneumatic devices. They are physically heavy, and those who have had them implanted are clearly aware of the 'machine in their chests'. An artist called Ollie Hirst [5] (a Gresham audience member) has congenital heart block and an implanted pacemaker. Despite the small size of modern pacemakers he is aware of the weight of the device and has created some stunning artwork, which demonstrates the feelings associated with this sensation of weight. Imagine what it must feel like to have a heart in your chest weighing several kilos.

Total implantable artificial hearts (TAH) also induce an enormous tissue reaction in the body. My colleague Steven Tsui in Papworth Hospital Cambridge, has removed a TAH to perform a transplant, and found the 'machine' surrounded by a 1" thick scar, which proved incredibly difficult to dissect. This adds greatly to the complexity of the operation and to the time a transplant takes.

You might reasonably assume that the total artificial heart has reached a relative dead end. There has been no fundamental change in the design of these hearts since the Liotta heart in 1969. Certainly, there have been improvements in the materials, power supplies and battery life. Advances in software controls and monitoring methods have also occurred, and it is surprising in a way that we are not further forward. Mortality remains high, and it is difficult to see at present why one might volunteer to receive one of these pulsatile devices.

Ventricular Assistance

Because of these issues and persistent and serious complications, the attention of researchers has largely become focussed not on total replacement of the heart, but on ventricular assist, since mostly it is the left

ventricle that is the dominant partner in terms of failure. Instead of removing the heart and replacing it *in toto*, why not take over the function of only the most seriously affected part of the heart, namely the left ventricle?

The principles of the pneumatically driven pulsatile membrane pump have been applied to isolated ventricular support, using a variety of devices, for example the Thoratec device, which began as a system in which the pump components of the heart is outside the body and the input and output pipes are connected to the left ventricle and aorta via long tubes. A more recent version can be implanted, with only the drive pipeline to the compressor being passed through the skin. The Thoratec device has mechanical valves and makes a distinctive (and loud) clicking sound.

A similar device is the Berlin Heart (EXCOR) [19-22], which also uses a membrane driven pump, in a clear housing outside the body. It has plastic, has silent valves and is small enough to use in children. And for some years it has revolutionised the management of children with severe heart failure who would otherwise have died on the waiting list for transplantation, children's hearts being so rarely donated. The quality of life for children on this device can be relatively good (they can play outside and learn in school), and they arrive for transplantation in due course in much better condition than they did in the days before such support existed. One of our patients has been attached to the device for a year waiting for a heart and, as you will see from the associated presentation, he is leading a remarkably happy life; despite is family having to spend most of their time in a hospital room. Such effective long-term support not only creates benefit, but also a problem. The machine is large and not suitable for 'care at home'. Specialist support needs to be close at hand. Our wards become full of patients waiting for a transplant and supported by a device. Organs are scarce and the queue grows, and in the current financial state of the NHS, such work displaces cases that would otherwise be treated by us. I will return to the implications of this later in the talk.

Whilst these pulsatile devices have obvious attractions, the complication rate remains significant and unpleasant, even though we have got much better at both minimising the incidence and mitigating the consequences. The incidence of clotting problems at various parts of the circuit, both in relation to valves and other complex nooks and crannies, has meant that obsessional anticoagulation management is required, with a variety of drugs and tests. It is not surprising that researchers have sought to find better ways of replacing the function of the ventricles of the heart.

Remember that the primary function of the heart is to pump blood around the body, and whilst our bodies have to use muscular contraction to propel blood from which a pulse must occur, general pump function is not contingent upon this, and most pumps are not pulsatile. Most are continuous flow, as you will know from your own central heating systems or the various pumps in a car engine. In terms of the heart, pumps of axial and centrifugal (impeller) design have become predominant in the market and recent advances in materials science, drive methods and bearing design have gone a long way to maximise efficiency and minimise blood damage [23]. These pumps are smaller, lighter, more durable and, as we shall see, result in better survival and less morbidity. For those wishing to read in more detail about the mechanics of these pumps, I recommend the excellent review by Moazami et al (2013)[23].

Both forms of pump have inlets and outlets, but the method of blood propulsion differs. Valves are not required because the pump mechanism itself permits flow in only one direction. The rotating element of a centrifugal pump is a spinning disk with blades that act as a 'thrower', meaning that fluid is captured and thrown tangentially outwards off the blade tips. The axial pump operates like a propeller in a pipe and acts more as a 'pusher'. Over recent years, there have been huge engineering advances in the design of the bearings, which support these rotating elements. Most axial pumps require mechanical pivot bearings, and most modern centrifugal pumps use electromagnetic or permanent magnet bearings, usually combined with hydrodynamic bearings, which keep a virtually frictionless surface layer of blood to separate the moving parts (see the pdfs of the slides of this presentation). Some newer axial pumps also use magnetic Centrifugal pumps are able to operate at a wide variety of flows for a very small change in pressure across the pump, and are easier to control because the current applied to them is linearly related to the flow. This can be exploited to generate some degree of pulsatility. Axial pumps have no such linear relationship between flow and current, so a variety of control sensors have to be added to the design. They also have lower flow pulsatility and an increased danger of suction effects on the left ventricle, pulling the septum across and potentially causing intracardiac valves, especially on the right, to leak.

Axial pumps also have a tendency to accumulate thrombus in low flow states and may need more aggressive anticoagulation, although new bearing designs and newer vane shapes may reduce the risk. Moazami concluded his paper in 2013 [23] by suggesting that current rotary pump designs have eliminated many of the theoretical disadvantages of axial pumps by having low shear bearings and good longevity and durability, a sensor less flow estimator (measuring current), an ability to withstand considerable shocks (e.g. car crash), reasonable pulsatility and the possibility of reduced anticoagulant dosage. Both axial and centrifugal pumps have overcome many of the challenges of biocompatibility, reliability and haemo-compatibility meaning that they have now become part of mainstream thinking in medicine. Indeed, continuous flow pumps now make up 97% of the 2500 ventricular assist devices implanted worldwide (2013 data), chosen because of their superior performance and freedom from adverse events. During the decade it has taken to complete this transition from pulsatile to continuous flow devices, the hospitalisation costs have fallen by 50%[24].

Survival after insertion of an LVAD now approaches the survival after successful heart transplantation, at least in the first few years (70% v 80%). And the patients do not have to take toxic drugs. It is not surprising that people are opting for such devices as a destination therapy, rather than running the risk of dying, waiting for an increasingly remote possibility of transplant. The ability to implant these devices with ever smaller (and quieter) power drive units has contributed to their attractiveness, and although single ventricular support is still the dominant 'market' for these products, improved software will undoubtedly allow matching of the outputs and rates of devices inserted into both right and left ventricles. There is room in the chest for both.

It would obviously be wonderful if the power supply could also be miniaturised and at best implanted with the device. We are some way from that but both private manufacturers and academic research units are researching a wide variety of power sources, up to and including nuclear, although not as far as I am aware using the gamma radiation that was tried first in Houston. There will be a breakthrough; battery design is so much better than it was even 10 years ago (except for my phone perhaps) and, if not yet longer lasting, batteries are certainly smaller and lighter.

Researchers are also considering the potential of biologic pumps based on newly resurgent stem-cell based regenerative medicine. This is a cornerstone of the Johns Hopkins artificial heart program where work is going on to develop biologic peristaltic pumps (based on principles for a synthetic larynx, also developed there), wrapping bioengineered muscle around the failing heart, or more distally around the aorta.

Success in the treatment of a disease present at such scale in the modern world generates problems that could become overwhelming. You don't have to be a rocket scientist to realise that if there are 25 million people with the problem and if a new, and obviously expensive treatment becomes available, it is probably a good idea to do a cost:benefit analysis. Ventricular assist is a rather telegenic technology, and has a Lazarus like effect on patients who are successfully treated, as you have seen. Demand will rise, and presumably costs will fall. But will health systems pay?

There have been a number of papers analysing the economic utility of this treatment, both in the UK and in the USA. The US data were most recently reported by Miller et al [25], and show that LVAD therapy is currently very expensive compared with other forms of treatment for heart failure, but they emphasise that costs are falling and quality of life rising. In the UK, cost benefit to the NHS and society is left to be judged by NICE, which advises commissioners on which treatments can be said both to work and to be affordable. Current NICE Guidelines[26] support the use of LVAD both as bridge and destination therapy, but regard it as in its relatively early stages and should be limited to dedicated teams. Patient selections should be careful and limited to those 'who are likely to derive sustained benefit in terms of survival and quality of life'.

NICE also notes that the 'technology for this procedure has evolved significantly in recent years and continues to do so'. Despite the success of the treatment internationally, in the UK only a relatively small number of these procedures are performed, about 100 per year, compared with over 1000 per year in Germany for a not dissimilar population. The ratio of VADs inserted to TAH insertions worldwide is in the order of 500:1, and one can see that the market for these products is growing, built on better and better results. Even greater benefit may occur if they are used slightly earlier in the course of disease, particularly in terms of quality of life. Peter Laussen has suggested (personal communication) that we add another concept of bridging to the list given earlier; bridge to decision. Keeping someone alive until everyone can come to terms with the death of the patient.

I have used the artificial heart as an example, but of course all technology dependence in medicine is expensive. Those who can afford it will always find a way of getting the support they need, but it should not be at the expense of the public system and the data associated with the work should still be collected and pooled.

I have a Dream

Actually it is a nightmare

Donald Trump. The Donald. I suspect that you will recognize him, and agree that he is both wealthy and vain. He is also entering an age group in which heart failure is likely to become a problem, especially with his stressful lifestyle. My nightmare is that he, and similarly rich oligarchs, would pay to have an artificial heart inserted; one proves to work. Unfortunately, for all of us the aging process continues and it is not unreasonable to think that he might become demented, have a stroke or develop cancer. Imagine that, rather than these diseases proving fatal, he survives - maintained by good nursing and expensive care. I rather suspect that he would want to be kept alive until a cure for his stroke or dementia could be identified.

The nightmare does not stop there. Imagine we have a ward full of 'people like him'; all with an artificial heart, all consuming vast amounts of resources which could be used to treat others, all with diseases which might be perceived by others as making their lives poorer, but all unable to die conventionally because their heart will just keep on going until it is turned off. By someone else.

And who has the **right** to turn it off? My nightmare is made more unpleasant by the realisation that people with his level of vanity are unlikely to have left an advance directive indicating the circumstances in which such an action would be acceptable. Trump's advance directive might be one which states that he does not want anyone to turn it off. The right to life is a moral principle based on the belief that a human being has the right to live and,

in particular, should not be killed by another human being. Article 2 of the Human Rights Act (1998) states: *Everyone's right to life shall be protected by law. No one shall be deprived of his life intentionally save in the execution of a sentence of a court following his conviction of a crime for which this penalty is provided by law.*

Under current law, a healthcare professional's legal duty is to care for a patient and to take reasonable steps to prolong their life. So how could we turn off Trump's machine, and under what circumstances? Although there is a strong presumption in favour of providing life-sustaining treatment, there are circumstances when continuing such treatment ceases to provide a benefit to the patient and is not clinically indicated. There is no legal distinction between withdrawing and withholding life-sustaining treatment. A person with **capacity** may decide either contemporaneously or by a valid and applicable advance decision that they have reached a stage where they no longer wish treatment to continue. If a person lacks capacity, this decision must be taken **in their best interests and in a way that reflects their wishes (if these are known).**

The legal principles around consent are the same for all medical interventions, including decisions to withdraw or withhold life-sustaining treatment. There is an important distinction between withdrawing or withholding treatment that is of no clinical benefit to the patient or is not in the patient's best interests, and taking a deliberate action to end the patient's life [6]. A deliberate action that is intended to cause death is unlawful. The debate about this issue clearly overlaps with wider debate about 'the right to die' and euthanasia, and it is worth reading the review of active and passive euthanasia by Rachels (1975)[27]. *Active euthanasia* occurs when the medical professionals, or another person, deliberately do something that causes the patient to die. *Passive euthanasia* occurs when the patient dies because the medical professionals either don't do something necessary to keep the patient alive, or when they stop doing something that is keeping the patient alive. Examples include, switching off life-support machines (including a circulatory pump such as an LVAD), disconnecting a feeding tube, not carrying out a life-extending operation and deciding not to give life-extending drugs.

Also in this context, there is much literature about the provision of adequate nutrition and hydration (ANH). The doctor's duty of care will require that they provide ANH while such treatment continues to prolong life. Where life depends upon the continued provision of ANH, ANH will be clinically indicated. If the patient lacks capacity, all reasonable steps that are in the person's best interests should be taken to prolong their life. Although there is a strong presumption in favour of providing life-sustaining treatment, there are circumstances when continuing or providing life-sustaining treatment stops providing a benefit to a patient and is not clinically indicated. (Burke v the General Medical Council [2005] 3 WLR 1132)

The problem comes with the concept of **futility**. The basic definition of medical futility is stated as; "*Care that is medically futile is that which is unlikely to produce significant benefit to the patient*"–. But as Eskildsen has said, in an interesting review of the topic[28], deciding what 'significant benefit' means has both moral and ethical implications. Continuing life which some might judge as 'futile' has economic implications too. A huge percentage (at least 30%) of the West's healthcare budget is spent in the last year of life, and developments in ventricular support or TAH are not going to reduce that proportion. Much of recent medical thinking is based on the 1990 paper by Schneiderman and colleagues[29], in which they defined futility to exist if, "in the last 100 cases a medical treatment had been useless".

We should consider by whose criteria 'useless' is defined. For example, if we judge futility from the clinician's perspective, this may be something that is not medically indicated, but may be valued by the patient. Conversely, something may be judged futile from the patient's perspective if it is medically indicated, but not valued by the patient. This concept of value is integral to much of modern medical (and social) thinking, and has been allocated its own 'term'; *value-based healthcare[30],* defined by Michael Porter as an equation thus;

value *(to the patient) =* **outcome** *of the care (over the course of life)*

cost *of care (over the course of life).*

Schneiderman et al [29] also distinguished two types of futility; *quantitative futility* in which a particular treatment is capable of producing a desired result, but is extremely unlikely to do so in the case in hand; and *qualitative futility* in which a treatment is likely to produce a result, but is 'lacking in purpose'. The latter is clearly more open to value judgments applied by the physician caring of the patient. Indeed Bagheri has argued[31] that it should be the *physician's* exclusive right to determine futility and to decide if treatment should be either withheld or withdrawn. Eskildsen rightly points out[28] that such definitive views can result in a moral and ethical standoff between family and physician. Bramstedt has specifically considered[32] the issue of turning off an artificial heart in the circumstances of futility. Her concluding comments are wise: *"All therapies, whether implanted or not, should be re-evaluated in cases in which the benefit is questionable, and in which suffering or death would be prolonged..... it is difficult to exclude TAH therapy as a form of aggressive care that could be ethically withdrawn in such cases. When beneficence cannot be facilitated, families and physicians must consider termination of this life support therapy."*

That, I imagine is where you, the public, come in. Who should determine futility; physicians; the family; and/or the courts?

I hope I have made it clear that the technology is marching on apace. Hardware and software are beginning to

match expectations, and may soon exceed them, but I do not think we have a moral, ethical or economic structure at present which could cope with success. Unlike many other life-sustaining or lengthening procedures, there is a fairly immediate problem of **scale.** There are huge numbers of patients in the world who, potentially, could benefit from this therapy. We have to address questions about **access;** who should be allowed the therapy? Should it be first come first served for a rationed resource, or should it be available only to the rich, those 1% who already hold 50% of the world's wealth? There are basic **economic** questions; is this a sensible development on any cost:benefit analysis? And who has the right to distribute the resources? There are **legal** questions; do our current legal rules deal adequately with these issues, and if not do we resolve it by case law or by some other method? What is the role of **faith**? All of us who work in intensive care with patients whose life is effectively over, but who are supported by one form of life maintaining treatment or another has been faced by a family's religious advisors who argue that everything is in God's hands, and many fundamental representatives of the world's religions take the view that there can be no withdrawal and in some cases no de-escalation of treatment. Under these circumstances, and with an effective pump, apparently futile life could go on for a very long time. Peter Laussen has suggested (personal communication) that we add another concept of bridging to the list given earlier; bridge to decision. Keeping someone alive until everyone can come to terms with the death of the patient.

It seems to me that we need to start debating these issues now. Many people and organisations will have strong and probably divergent views. The technology will not stop evolving, and industry, clinicians and many patients clearly have a vested interest in its acceptance and application. As Tannsjo has said [33] '*Modern medicine has prolonged not only our lives but also our period of dying*'. If we do not plan ahead, anarchy will ensue and demand will exceed supply. NICE clearly has a role to review the data available at regular intervals, but the ethical and moral issues need public engagement in the same way that there was debate about human fertilization and embryology, led by Dame Mary Warnock in 1984. I would like to use this lecture to make a plea for such an approach before it is too late.

And we are still left with my nightmare; what are we going to do with our everlasting Donald Trump? Or Putin, or Al Assad, or Kim Jung Un, or……

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[4] http://www.medgadget.com/2005/07/paul_winchell_a.h...

[5] www.olliehirst.co.uk

[6] For a full list of relevant cases and case law visit http://www.gmc-uk.org/guidance/ethical_guidance/end_of_life_legal_annex.asp which the General Medical Council legal team have kindly collated.