

THE CARDIAC PIONEERS OF GUY'S

*Advances in heart surgery were among the great medical successes
of the past century, and Guy's surgeons were in the thick of it*

SIR TERENCE ENGLISH

He performed the UK's first successful heart transplant. Thirteen heart recipients attended his retirement party; between them, they had lived 130 years beyond their operations





LORD RUSSELL BROCK

Lord Brock, seated at centre, and his staff following completion of his 100th pulmonary valvotomy. He cared deeply for his patients, 'and those early failures and deaths caused him great anguish', says Professor Cooper

'The heart is a wonderful pump. But that's really all it is. It pumps blood through the lungs, where it gets oxygenated, and then pumps the oxygenated blood around the body.'

At the same time, Sir Terence English is quick to add, the heart is an awe-inspiring bit of evolution, never at rest from before birth to our final day.

Retired from his successful career as a cardiac surgeon, Sir Terence knows the heart about as well as anyone. He was one of a small number of people who pioneered heart surgery in the 20th century – a group of driven, competitive visionaries who pushed the boundaries to repair, and even replace, an organ that much of the medical profession had considered off limits until a few decades ago.

Yes, Egyptians more than 2,000 years ago recognised the importance of the heart's pumping action. Its steady, almost mystical rhythm made it a remarkable part of the body. Despite – or maybe because of – its clear importance, most surgeons until the mid-20th century feared to take a scalpel to this 'mansion of the soul'.

'Some cardiologists in the 30s, 40s and even

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Many surgeons believed the heart couldn't tolerate surgery

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into the 50s were very, very sceptical about surgeons operating on the heart,' says Sir Terence. 'Many felt it was too dangerous, that the heart would not stand being operated on.'

In a span of four decades all fear and superstition surrounding the heart were swept aside: doctors discovered the heart could tolerate surgery. This year marks the 60th anniversary of the first successful open heart surgery,

and the 45th anniversary of the first transplant.

Most of the doctors who developed procedures such as hypothermic surgery and inventions such as the heart-lung machine

were North Americans. However, several surgeons who trained or worked at Guy's Hospital figure prominently in this story, and this article focuses on four of them, all connected to one another: Lord Russell Brock, who realised several significant cardiac achievements in the 1940s and 50s and was made a lord in 1965; Donald Ross, a leading innovator in the 60s and, according to Sir Terence, 'the finest cardiac surgeon of his generation'; Sir Terence, who performed the UK's first successful heart transplant in the late 70s; and David Cooper, who continues to work as Professor of Surgery at the Thomas E Starzl Transplantation Institute at the University of Pittsburgh Medical Center.

Two of these gentlemen have written about advancements in cardiac surgery. Sir Terence's autobiography, *Follow Your Star*, includes details about the heart transplant programme he established at Papworth Hospital near Cambridge. Cooper's book, *Open Heart: The Radical Surgeons Who Revolutionized Medicine*, traces advancements in heart surgery from the 1930s, when surgeons first operated on blood vessels close to the heart,

to creation of the controversial Jarvik artificial heart in the 1980s. Through interviews with dozens of physicians and his own experiences – he worked with Lord Brock and Ross and assisted with Sir Terence's first transplants – Professor Cooper details scientific developments and explores the surgeons' personal lives.

A STREAK OF SHOWMANSHIP

Innovative, demanding and intimidating, Russell Brock pushed his staff to wits' end and exhaustion. A 1927 Guy's graduate, Lord Brock emerged as a leading cardiac surgeon shortly after World War II. Professor Cooper describes him as an introspective perfectionist 'with a streak of showmanship'. He is recognised for several contributions to cardiac surgery, including advances in relieving mitral valve stenosis and inventing a mechanical valve dilator. His groundbreaking pulmonary valve operation saved lives by opening narrowed valves; this alleviated the problem of 'blue babies', children who suffered from an obstruction of blood flow to the lungs. This operation also 'demonstrated the heart's tolerance to direct surgical intervention', writes Professor Cooper.

'Sir Thomas Holmes Sellors actually did the operation about a week before, but Brock got it into the literature first,' says Sir Terence. 'People like Brock and Sellors were very competitive. And they were prima donnas in the operating room. There's no doubt about it.'

Professor Cooper writes about Lord Brock's brusque behaviour but in a sympathetic light. Like every physician pushing the boundaries of cardiac surgery in the mid-20th century, Lord Brock regularly saw patients die on the operating table; despite extensive testing on dogs and other animals, mortality rates were high, which 'must have given him many sleepless nights.'

By the time Professor Cooper arrived at Guy's as a student, Lord Brock's star was being eclipsed by younger colleagues, such as Ross, who were adept at open heart surgery, whereas Lord Brock was much more at ease with closed heart surgery. Still, students were in awe of the man. Professor Cooper remembers skipping lectures to watch him perform in the operating theatre.

NEVER LOSING HIS COOL

Ross, a native of South Africa, graduated first in his medical class at the University of Cape Town, a class that included Christiaan Barnard. He joined Guy's Hospital in 1952 and became Lord Brock's senior registrar. 'He and Brock complemented each other,' says Sir Terence. 'But Donald was different. He was a superb technician and never lost his cool in the operating room.'

While working at Guy's, Ross developed a complex operation, still performed worldwide and known as the Ross procedure, in which the surgeon uses the patient's own pulmonary valve to replace the diseased aortic valve, and then puts an aortic homograft from a deceased donor into the pulmonary position. This pioneering work, says Professor Cooper, stimulated research into heart valve replacement, including the use of pig valves. Ross is also credited with performing the first total correction of tetralogy of Fallot – a common cause of blue baby syndrome – on a patient younger than a year old, in 1961. This patient is alive today and is the longest-lived survivor of this operation in the world – a remarkable example of translational medicine.

Ross was part of a generation working toward an operation that at one time seemed unthinkable: total replacement of a damaged human heart. While surgeons had shown that the heart could withstand surgery, taking one person's heart and placing it into another individual's body presented an entirely different level of complexity. Introduction of foreign tissue triggers an immune response; it's the body's way of protecting itself from pathogens such as viruses and bacteria. Most cardiac surgeons in the mid-1960s expected Norman Shumway of Stanford to attempt the first transplant, as he appeared to be making the greatest progress toward developing immunosuppressants to protect a donor heart. Barnard surprised everyone in December 1967 when he performed the world's first heart transplant, becoming the medical profession's rock star. Within a short time, says Sir Terence, people living deep in the Amazon rainforest knew the name Christiaan Barnard.

'I visited Barnard in 1963. Donald Ross said, "Go and see what that crazy guy Barnard is doing in Cape

A few other pioneers...

To list every physician at Guy's, King's College Hospital, King's College London and St Thomas' who contributed to better heart care during the past century would fill an entire issue of *In Touch*. Other notables include:

- **Henry Barcroft**, of St Thomas', studied the physiological effects of haemorrhage and developed an instrument to measure the rate of blood flow.
- Working at Guy's Hospital during World War II, **Ronald Thompson Grant** studied the physiology and pathology of blood vessels and the effects of haemorrhage on circulation.
- Guy's **Edgar Sowton** was a pioneer in the creation of the cardiac pacemaker. He was one of the first surgeons in the UK to perform coronary angioplasty, keyhole surgery on the arteries of the heart.
- **Ernest Starling**, of Guy's, is remembered for 'Starling's Law', which states that 'the energy of contraction is a function of the length of the muscle fibres'. He also discovered secretin and coined the term 'hormone'.

Town,'" Sir Terence recalls. 'So I spent a week with him and was singularly unimpressed. He was certainly a good surgeon and he was getting excellent results, but his behaviour in the operating room was bad. He would shout and blame his assistants.'

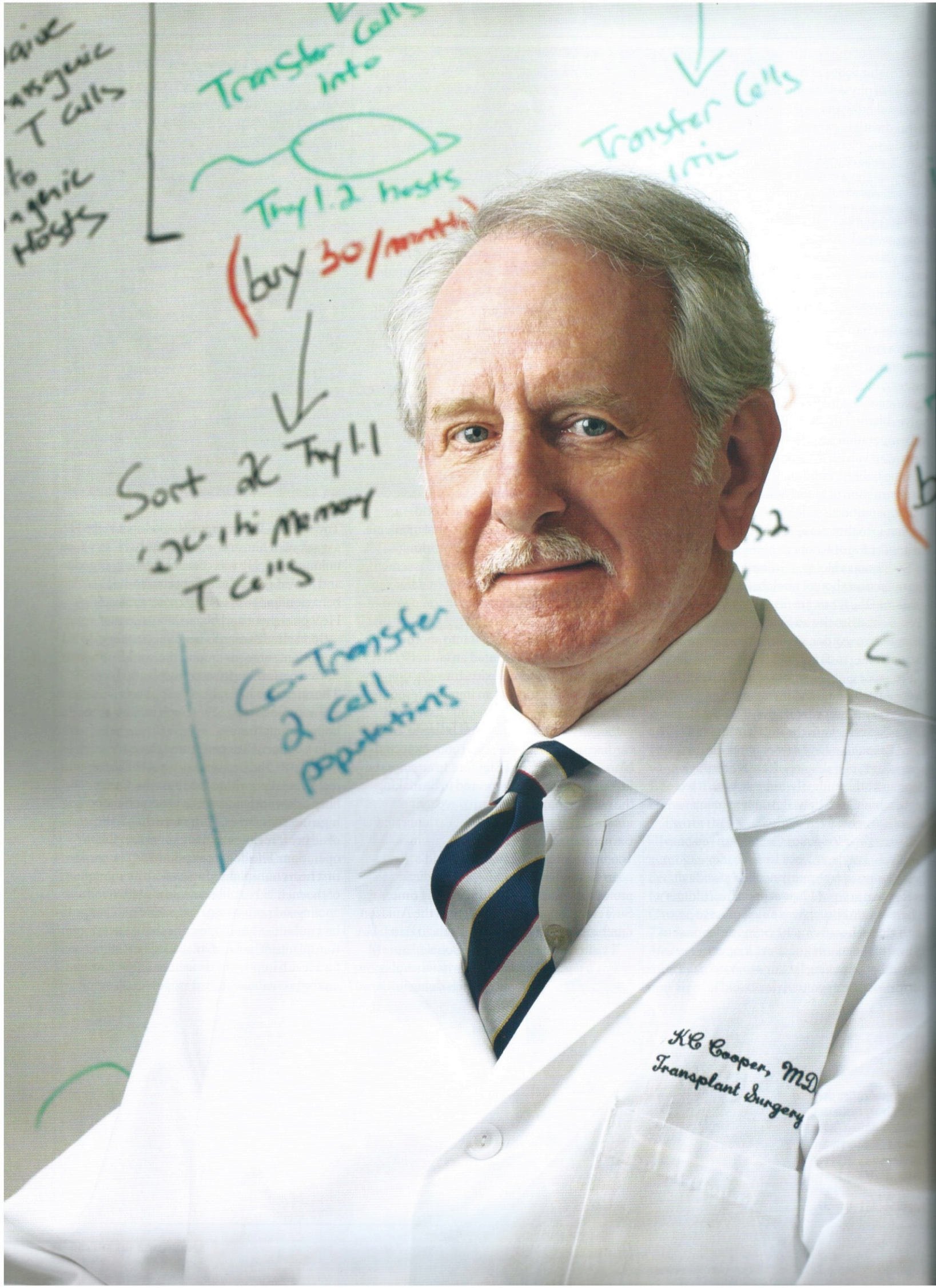
Soon after Barnard's headline-making operation, surgeons around the world started performing heart transplants. The operation had seized the public's attention and inspired research into new immunosuppressants.

In London, Ross performed three transplants, the first in May 1968; all three recipients died within four months. Other hospitals worldwide were also experiencing high mortality rates, with more than half of all heart recipients dying soon after the operation. The hoopla surrounding Barnard's first heart transplant soon settled: members of the medical establishment wanted a cooling-off period and the general public had questions about the ethics of heart transplants. The UK Chief Medical Officer for Health imposed a de facto moratorium on the procedure.

DONALD ROSS

Ross's generation pursued the unthinkable: heart transplantation. 'He was, I believe, the foremost cardiac surgeon of his generation,' says Sir Terence. Nearing 90, Ross lives in London





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HB Cooper, MD
Transplant Surgery

SUCCESS IN THE UK

Like Ross, Sir Terence grew up in South Africa. He was the son of a mining engineer and nephew of a surgeon; both careers intrigued him. He tried mining first, taking a job at age 17 to work as a diamond driller in what was then called Rhodesia. 'I played poker, drank brandy and did all the sort of things you do when you're growing up,' he recalls. He started a course of study in mining engineering but in his third year he inherited 'a little legacy' of £2,000. Following several conversations with his uncle, he decided to pursue a career in medicine after completing his engineering studies.

When he first qualified he worked with Dr Charles Baker, senior cardiologist at Guy's, and then trained with Lord Brock. He assisted on two of Ross's early homograft operations before moving to Papworth to establish its reputation as one of the UK's premier cardiac programmes. He collaborated with Professor Sir Roy Calne, another Guy's alumnus and Brock trainee who became one of the world's leading experts in immunosuppression while performing liver transplants in Cambridge.

Sir Terence also found himself enmeshed in ethical and religious debates over the definition of death. A surgeon needs a working heart for a successful heart transplant. For many, it was simply wrong to remove a beating heart from a body. Others argued that death should be defined by whether brain death had occurred, not by heart activity. A 1976 report by the Medical Royal Colleges opted for the latter and laid out a series of simple tests that allowed a physician to determine whether a person was brain-dead or not. 'The brain stem is at the base of the brain, and all the important connections are in the brain stem,' says Sir Terence. 'If the brain stem is destroyed you don't breathe, and if you don't breathe you die. So one of the tests for brain death is whether there's spontaneous respiration if a person is taken off a ventilator.'

After much experimental work, Sir Terence submitted his heart transplant protocols in 1977. The Department of Health's Transplant Advisory Panel replied that it didn't have funds for a programme and didn't want 'any one-off operations'. Undeterred, he sought out another source and secured funding for two

transplants through the Area Health Authority in Cambridge. Unfortunately, the first recipient patient suffered cardiac arrest as he was being prepared for the operation, while Sir Terence was in another hospital removing the donor heart, the most complex aspect of the procedure. Soon after the operation was complete it became clear that the patient had suffered brain damage. He died 17 days later from an infection.

'The Department of Health was pretty angry,' Sir Terence recalls. He pressed on and by late summer 1979 he had lined up 'a very good donor heart' but a less-than-ideal recipient: Keith Castle, a 52-year-old smoker suffering from vascular disease and an intestinal ulcer.

'But he had a wonderful character. He was a Wandsworth cockney and he just sailed through the operation,' says Sir Terence. 'Keith probably did more to advertise the potential benefits of cardiac transplantation than ever I could have done. He was a great cyclist and got involved in all sorts of activities, fundraising for the hospital and promoting organ donation.'

By the time he retired, Sir Terence had led or assisted in more than 200 heart or heart-lung transplant operations. Today, more than 3,000 heart transplants are performed each year around the world, with a success rate approaching 90 per cent.

GENETIC MODIFICATION

Professor Cooper, a 1963 Guy's alumnus, was present at Ross's first heart transplant and assisted Sir Terence with his first four transplant operations. He then worked with Barnard for several years in Cape Town. Today, he is an internationally recognised expert on xenotransplantation – transplanting an organ from one species to another.

'I realised back in the 1980s that we would never have enough hearts for all the patients who needed a transplant,' says Professor Cooper, who gave up surgery for research in the mid-90s. It's a problem for other forms of transplantation, as well, he says. In the United States alone there are more than 110,000 people waiting for an organ transplant, and only about 30,000 organs become available annually. Many die each year waiting for

a heart, kidney, liver or other organ.

Several surgeons in the 1960s and 70s transplanted hearts from baboons and chimpanzees, each operation unsuccessful due to the recipient's immunological response. Xenotransplantation research in recent years, however, has zeroed in on pigs. Surgeons have been replacing damaged elements of the human body with pig parts for decades – John

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Wayne was given a pig heart valve back in 1978 – but the push now is to genetically engineer pigs to reduce the human body's immunological reaction.

Surgeons are a few years away from putting an entire pig heart into a man or woman, Professor Cooper predicts. However, he says, researchers are close to carrying out clinical trials on transplanting

genetically modified porcine pancreatic islets into humans, potentially a tremendous leap forward in the treatment of diabetes, as islets are necessary for the production of insulin. He adds that corneal transplants using genetically engineered pig sources are also not too far in the future.

Professor Cooper says he has enjoyed his career immensely as well as the writing he has done on the side. He is disappointed, however, that several of the pioneers in his book – the cardiac surgeons who overcame immense medical challenges to repair the heart – never received the widespread public recognition they deserved, despite the fact that their advances have saved countless lives.

'It's disgraceful,' he says, 'that none of them was awarded a Nobel Prize for open heart surgery.'

Sir Terence's book, Follow Your Star, is available from Authorhouse. Professor Cooper's Book, Open Heart, is published by Kaplan.

DAVID COOPER

A globally recognised expert in xenotransplantation, he believes that with enough genetic modification, a pig organ may eventually be more readily accepted than an organ from another human