

WELLCOME WITNESSES TO TWENTIETH CENTURY MEDICINE

EARLY HEART TRANSPLANT SURGERY IN THE UK

THE TRANSCRIPT OF A WITNESS SEMINAR HELD AT
THE WELLCOME INSTITUTE FOR THE HISTORY OF MEDICINE,
LONDON, ON 10 JUNE 1997

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WITNESS SEMINAR TRANSCRIPT EDITED BY:

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TECHNOLOGY TRANSFER IN BRITAIN: THE CASE OF MONOCLONAL ANTIBODIES; SELF AND NON-SELF: A HISTORY OF AUTOIMMUNITY;
ENDOGENOUS OPIATES; THE COMMITTEE ON SAFETY OF DRUGS • MAKING THE HUMAN BODY TRANSPARENT: THE IMPACT OF NMR
AND MRI; RESEARCH IN GENERAL PRACTICE; DRUGS IN PSYCHIATRIC PRACTICE; THE MRC COMMON COLD UNIT • EARLY HEART
TRANSPLANT SURGERY IN THE UK • HAEMOPHILIA: RECENT HISTORY OF CLINICAL MANAGEMENT •

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EARLY HEART TRANSPLANT SURGERY IN THE UK

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INTRODUCTION

The first human heart transplant challenged human concepts of individuality and the place of mankind in the same way as did the first pictures of Earth as seen from outer space – powerful, laudable, technical achievements that strangely disturbed, distorted, and disrupted the sense of self.

This Witness Seminar gathered together some of the key players in the early heart transplant operations in the UK, to discuss and debate the events of those days and their implications. Thus we learn not only of the surgical advances, heralded by the work of Shumway and Lower in Palo Alto, California, somewhat precipitately advanced by Christiaan Barnard in Cape Town, South Africa, and inaugurated in Britain by Donald Ross and colleagues, but also of the professional, social and legal disquiet at what, by the end of the twentieth century, has become an almost routine operation for many cardiovascular surgeons. We discover the divisions between medical professionals – the divergent views of surgeons, cardiologists, anaesthetists, and hospital administrators – all grappling with the momentous events overwhelming them. The role of the Press, in hounding the families of early donors, the recipients and the medical teams, was an unexpected complication, upon which many participants cast a rueful glance. Could a more sensitive awareness of the power of public relations have facilitated the progress of the heart transplant programme in Britain? Or were the medical problems so immense that the voluntary clinical moratorium was inevitable? Was the introduction of anti-rejection medication, most notably cyclosporin, already well used in kidney transplant surgery, the key development that made the ‘heroic’ surgery possible?

Readers will find several answers to these questions – the raw data of history is not neat and consistent, but it is rich and fascinating. Here we have from the major participants and others, several of whom were in junior, spear-carrying roles at the time, eye-witness accounts of what they saw, thought and believed.

Witness Seminars reflect the messiness of first-hand history – we provide the opportunity for those involved in particular events or discoveries to meet together to reminisce in what has become known as ‘open-peer review’, with comments and views immediately open to rejoinder and contradiction from fellow participants. The transcripts of the meetings are lightly edited to transform the spoken into the written word and explanatory bibliographical and biographical footnotes are added. Throughout, we remain in regular contact with all

participants – they see every change, have the opportunity to alter, modify, or add to their contributions. Stylistic alterations are made without note; more detailed amendments are added to footnotes, and all correspondence, tapes, and transcripts are deposited, with the participants' permission, in the Contemporary Medical Archives Centre of the Library of the Wellcome Institute for the History of Medicine.

To date, 21 Witness Seminars have been organized by the Wellcome Trust's History of Twentieth Century Medicine Group, most of which have been published. These are listed in the Table below. For the Heart Transplant meeting Lois Reynolds and I are especially grateful to Professor Tom Treasure for suggesting this meeting, assisting us in organizing it and for chairing it so successfully. We also thank Dr John Henderson for his comments and criticisms on the near-final manuscript; Dr Simon Joseph for providing the clinical details and description on pages 13–14; *Private Eye* for permission to reproduce the front cover of their issue of 5 July 1968; and Julie Wood for design assistance. As ever, we are indebted to the Publishing Department of the Wellcome Trust for their help, to the Medical Photographic Library and the Audiovisual Department of the Wellcome Trust, to Mrs Jaqui Carter, who transcribes the meetings, to the Wellcome Trust for their financial support of this programme, and to our colleagues, Dr Daphne Christie and Mrs Wendy Kutner, who join with us in running these meetings. But most especially we are grateful to all those who participated in the meeting, painstakingly read through several versions of the transcript, patiently answered our questions and provided additional information and material.

Tilli Tansey

Wellcome Institute for the History of Medicine

History of Twentieth Century Medicine Witness Seminars, 1993–1999

- 1993 **Monoclonal antibodies**¹
Organizers: Dr E M Tansey and Dr Peter Catterall
- 1994 **The early history of renal transplantation**
Organizer: Dr Stephen Lock
- Pneumoconiosis of coal workers**²
Organizer: Dr E M Tansey
- 1995 **Self and non-self: a history of autoimmunity**¹
Organizers: Sir Christopher Booth and Dr E M Tansey
- Ashes to ashes: the history of smoking and health**³
Organizers: Dr Stephen Lock and Dr E M Tansey
- Oral contraceptives**
Organizers: Dr Lara Marks and Dr E M Tansey
- Endogenous opiates**¹
Organizer: Dr E M Tansey
- 1996 **Committee on Safety of Drugs**¹
Organizers: Dr Stephen Lock and Dr E M Tansey
- Making the body more transparent: the impact of nuclear magnetic resonance and magnetic resonance imaging**⁴
Organizer: Sir Christopher Booth

¹ Published in Tansey E M, Catterall P P, Christie D A, Willhoft S V, Reynolds L A. (1997) (eds) *Wellcome Witnesses To Twentieth Century Medicine*, vol. 1. London: Wellcome Trust, 135pp.

² P D'Arcy Hart, edited and annotated by E M Tansey. (1998) Chronic pulmonary disease in South Wales coalmines: An eye-witness account of the MRC surveys (1937–1942). *Social History of Medicine* 11: 459–468.

³ Lock S P, Reynolds L A, Tansey E M. (eds) (1998) *Ashes to Ashes – The history of smoking and health*. London: Wellcome Trust, 198–220.

⁴ Tansey E M, Christie D A, Reynolds L A. (eds) (1998) *Wellcome Witnesses to Twentieth Century Medicine*, vol. 2. London: The Wellcome Trust, 282 pp.

- 1997 **Research in general practice**⁴
 Organizers: Dr Ian Tait and Dr E M Tansey
- Drugs in psychiatric practice**⁴
 Organizers: Dr E M Tansey and Dr David Healy
- The MRC Common Cold Unit**⁴
 Organizers: Dr David Tyrrell and Dr E M Tansey
- The first heart transplant in the UK**⁵
 Organizer: Professor Tom Treasure
- 1998 **Haemophilia: aspects of clinical management**⁶
 Organizers: Dr E M Tansey and Professor Christine Lee
- Obstetric ultrasound: historical perspectives**
 Organizers: Dr Malcolm Nicolson, Mr John Fleming and Dr E M Tansey
- Post-penicillin antibiotics**
 Organizers: Dr Robert Bud and Dr E M Tansey
- Clinical research in Britain, 1950–1980**
 Organizers: Dr David Gordon and Dr E M Tansey
- 1999 **Intestinal absorption**
 Organizers: Sir Christopher Booth and Dr E M Tansey
- The MRC Epidemiology Unit (South Wales)**
 Organizers: Dr Andy Ness and Dr E M Tansey
- Neonatal intensive care**
 Organizers: Professor Osmund Reynolds, Dr David Gordon and Dr E M Tansey
- British contributions to medicine in Africa after the second world war**
 Organizers: Dr Mary Dobson, Dr Maureen Malowany, Dr Gordon Cook
 and Dr E M Tansey

⁵ Tansey E M, Reynolds L A. (eds) (1999) Early heart transplant surgery in the UK. *Wellcome Witnesses to Twentieth Century Medicine*, this volume.

⁶ Tansey E M, Christie D A. (eds) (1999) Haemophilia: Recent history of clinical management. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 4. London: The Wellcome Trust, 81 pp.

EARLY HEART TRANSPLANT SURGERY IN THE UK

The transcript of a Witness Seminar held at the Wellcome Institute
for the History of Medicine, London, on 10 June 1997

Edited by L A Reynolds and E M Tansey

EARLY HEART TRANSPLANT SURGERY IN THE UK

Participants

Sir Christopher Booth	Professor Donald Longmore
Professor John Bunker	Dr Geoffrey Rivett
Dr David Carnegie	Mr Barry Ross
Sir Terence English	Mr Donald Ross
Professor Renée Fox	Sir Keith Ross†
Dr Alan Gilston*	Dr Jane Somerville
Dr Arthur Hollman	Dr Walter Somerville‡
Dr Simon Joseph	Professor Tom Treasure (Chair)
Professor Maurice Lessof	Dr David Tyrrell§
Dr Eunice Lockey	Mr John Wallwork

[updated 19 January 2005]

* died 18 June 2005

† died 18 February 2003

‡ died 20 July 2005

§ died 2 May 2005

Others present at the meeting: Dr Peter Fleming, Mr John Gibbons, Mr Raymond Hurt, Miss Anne Robertson, Mr Marvin Sturridge, Dr Raymond Vale, Professor John West

Apologies: Professor Dick Batchelor, Professor Sir Roy Calne, Mr David Cooper, Mr Tony Dyde, Sir George Godber, Professor James Mowbray

Professor Tom Treasure:¹ I am a cardiothoracic surgeon who was only a medical student when these important events were taking place, and I am here, not as a Witness but as the Chairman. That comes about because a couple of years ago I spent a most enjoyable four months' sabbatical working here at the Wellcome Institute and remained on in spirit as a member of the Steering Committee of the History of Twentieth Century Medicine Group, which runs these Witness Seminars.² The purpose of these is to get together people who were the witnesses, the key players, in important events in medicine within our memories, that is, within your memories, and to encourage you to talk about them and to tell us the things you remember and to get a dialogue going. It will be recorded and I would like people to give their names as they speak. Everybody who speaks will get a transcript, and nothing will be published that you would not want to be, and we hope that this will provide a very important, valuable and interesting account of these operations. We will have tea half way through the afternoon. After tea we will discuss the issues of what appears to have been a clinical moratorium, implicit or explicit, over a period of time, how that was negotiated, how it was dealt with and how it then changed.

But the first job is to think about the two operations that were done in London. The first operation was performed at the National Heart Hospital on 3 May [1968] and the first leader on the subject appeared in the *British Medical Journal* on 11 May 1968. The publication being so prompt was unusual. They could not have got it out sooner, and it was obviously regarded as a major event at the time. It says:

On the third of May the tenth heart transplant in the world was successfully accomplished at the National Heart Hospital, London. Mr Donald Ross, Mr J K

¹ Professor Tom Treasure FRCS (b. 1947) trained in London and the USA, and has held a personal chair in Cardiothoracic Surgery in the University of London at St George's Hospital since 1994.

² As part of the Wellcome Trust's initiative to encourage research in the history of twentieth century medicine and medical science, a scheme has been developed for academically based clinicians or scientists who wish to undertake a short period of full-time research to learn the methods of historical scholarship and to explore the wider determinants and contexts of their own medical and scientific work. Further details available from the History of Medicine Programme Manager at the Wellcome Trust.

Early Heart Transplant Surgery in the UK

Ross and Mr Donald Longmore and their team deserve the congratulations of their colleagues on the success of their first human transplant.³

It was met with acclaim and those three named gentlemen are all here. The operation was reported in a symposium on human heart transplantation in the *American Journal of Cardiology* in December 1968, and interestingly, the opening quotation is from Sir Peter Medawar who said at the time, in September 1968:

The transplantation of organs will be assimilated into ordinary clinical practice...and there is no need to be philosophical about it. This will come about for the single and sufficient reason that people are so constituted that they would rather be alive than dead.⁴

It is fascinating that he should have said that at the time, and of course we who are here now know that the only limit on the number of heart transplantations done in this country, and in most countries in the world, is the number of available donor organs. In a way, that is just as well for the time being, because otherwise the explosion of that practice would be huge. So heart transplantation now is very much part of our routine practice, and part of the treatment of that stage of ventricular failure. That's the stage we have got to.

What I would like to do is call upon several individuals to make a start and tell us their recollections of the event and say as little or as much as you like, although there will be plenty of time to come back and discuss further. Mr Donald Ross, would you like to start and tell us about the operation and what was happening at the National Heart Hospital?

Mr Donald Ross:⁵ I am not sure exactly what you want to know, because we were concerned with trying to get a heart transplant going for some time before the actual operation. We were all keyed up, we knew about it, we had a patient, we had got a donor and we did a transplant, and it worked surprisingly well, initially anyhow. I suppose, as one of a group of people doing heart transplants at that time, that the concept originated much earlier. Surgeons in general, all cardiac surgeons, were aware of the need for a transplant and were able to do a transplant

³ Anon. (1968) First British heart transplant. *British Medical Journal* ii: 315.

⁴ From Sir Peter Medawar's speech at the Second International Congress of the Transplantation Society, 11 September 1968, New York City, in Kantrowitz A, Haller J D. (eds) (1968) Symposium on Human Heart Transplantation: Introduction. *American Journal of Cardiology* 22: 761–765, quote on page 761.

⁵ Mr Donald N Ross FRCS (b. 1922) was Consultant Cardiac Surgeon (now Emeritus) at the National Heart Hospital (now the Royal Brompton National Heart and Lung Hospital), London, from 1963 to 1993, and at Guy's Hospital, London, from 1958 to 1978. See Ross D. (1968) Report of a heart transplant operation. *American Journal of Cardiology* 22: 838–839.

technically. They had been practising in the laboratories for some time. I would like to come back to the father figures in this area, Messrs Shumway and Lower of Palo Alto, California, near San Francisco, had been scientifically working on transplantation of the heart in animals.⁶ We were all playing around with it technically only and were excited about sewing in the heart, which is in fact when you come to think about it, quite a simple plumbing job. Our friend and my colleague, Christiaan Barnard,⁷ went to visit Palo Alto, saw it, came back through London and said, 'I am going to do that'. Lo-and-behold, within a couple of months he did it. He had the courage to do it, but the background knowledge belongs to the Shumway group, there's no doubt about that. We were just following, like sheep in the background. We all did the operation because they showed us the way, and Barnard had the courage to do it first. I think that's all I have got to say at this stage.

Treasure: Professor Donald Longmore, you were one of the surgeons involved, as named in the editorial of the *British Medical Journal*. Can you tell us a bit more about the process, the thinking?

Professor Donald Longmore:⁸ Yes, indeed. I think Donald [Ross] has been rather modest about the whole thing. First of all, we were all aware that Alexis Carrel had done an experimental heart transplant in 1905 and that Demikhov had done a series in 1952 and we were also aware that Shumway was doing research in this area.⁹ We applied for a British Heart Foundation grant, Sir

⁶ Norman Shumway (b. 1923), surgeon, moved to Palo Alto in 1957. Richard Lower (b. 1929), surgeon, moved to Palo Alto in 1958. See Lower R R, Shumway N. (1960) Studies on the orthotopic homotransplantation of the canine heart. *Surgical Forum* 11: 18–19. Lower R R, Stofer R C, Shumway N E. (1961) Homovital transplantation of the heart. *Journal of Thoracic and Cardiovascular Surgery* 41: 196–204. See also Dong E, Shumway N E, Lower R R. (1991) A heart transplantation narrative: The earliest years. In Terasaki P. (ed.) *History of Transplantation: Thirty-five recollections*. Los Angeles, CA: UCLA Tissue Typing Laboratory for the Regents of the University of California, 435–449.

⁷ Professor Christiaan Barnard (1922–2001) has been Senior Consultant and Scientist in Residence at the Oklahoma Heart Centre, Baptist Medical Centre, since 1985. He was Professor of Surgical Science at Cape Town University from 1968 to 1983, Professor Emeritus from 1984. He performed the world's first human heart transplant operation on Louis Washkansky at the Groote Schuur Hospital, Cape Town, South Africa, on 3 December 1967. [updated 19/1/06]

⁸ Professor Donald Longmore OBE FRCSEd FRCR (b. 1928) was Professor of Magnetic Resonance in Medicine and Director of the MR Unit, Royal Brompton National Heart and Lung Hospital, London, from 1982 to 1993, now Emeritus. He is Director of Brompton MR Enterprises and Chairman of MR3000, a company producing advanced magnetic resonance equipment. He was Consultant Surgeon and Clinical Physiologist at the National Heart Hospital from 1963 to 1980.

⁹ Alexis Carrel was awarded the Nobel Prize in Physiology or Medicine in 1912 for his method of suturing blood vessels, which permitted artery replacement. See Carrel A, Guthrie C C. (1905) The transplantation of veins and organs. *American Medicine* 10: 1101–02. During the 1940s and

Thomas Sellors¹⁰ and me, in 1963, and we were told that the roars of laughter could be heard two or three blocks away. In late 1963, we got a grant of £6000, which in those days was a very large sum of money and I rented a laboratory in the Royal Veterinary College for six old pence a year, and we set about what we thought was a very scientific approach and we were also supported by the Wellcome [Trust]. David Long, who was the father of *Imuran*,¹¹ and we, actually did a very large number of dogs, but only doing heart–lung transplants. We also did dog to sheep, sheep to dog, sheep to pig, and a whole lot of cross-species transplants. After we had been going a while, the Royal Veterinary College establishment realized what was going on and took legal advice from McFarlanes, the solicitors. McFarlanes investigated the whole thing and told the Vet College that they were so out of date that they could only benefit from having active, progressive surgeons in the place, and that they mustn't shut us down. Following that, we were working there assiduously, and Chris Barnard, whom Donald has mentioned, visited us twice, as did a group from the Hammersmith, one of the DeBonos¹² was trying to do similar work at the Hammersmith. I forgot to

1950s Vladimir Petrovich Demikhov performed many transplantations on dogs at the M V Lomonosov Moscow State University. See Demikhov V P. (1962) *Experimental Transplantation of Vital Organs* [B Haigh (trans)]. New York: Consultants Bureau. Russian text published by State Press for Medical Literature in 1960. For a general review of early work in cardiac surgery, see Tröhler U. (1998) From Rehn's risky cardiac suture (1896) to routine cardiac transplantation (1996): Historical and ethical perspectives. *Journal of Cardiovascular Surgery* 39: 7–22.

¹⁰ Sir Thomas Holmes Sellors (1902–1987) was Emeritus Surgeon at the Middlesex Hospital, Honorary Consulting Surgeon to the National Heart Hospital, Consulting Surgeon at the London Chest Hospital, Harefield Hospital and Benenden Chest Hospital. He was President of the Royal College of Surgeons from 1969 to 1972. See Sellors T H. (1967) The genesis of heart surgery. *British Medical Journal* i: 385–393.

¹¹ Dr David Long was head of the Medical Research Division and from 1968 to 1972 Director of the Wellcome Research Laboratories, Beckenham, Kent. Azathioprine (*Imuran*, Wellcome), a derivative of 6-mercaptopurine, is an immunosuppressant widely used for transplant recipients. See Calne R Y, Alexandre G P, Murray J E. (1962) A study of the effects of drugs in prolonging survival of homologous renal transplants in dogs. *Annals of the New York Academy of Science* 99: 743–761. Gertrude Belle Elion (1918–1999) and George Hitchings (1905–1998) shared the 1988 Nobel Prize in Physiology or Medicine with Sir James Black, for their drug discoveries. For the development of 6-mercaptopurine, see Elion G B. (1993) The quest for a cure. *Annual Review of Pharmacology and Toxicology* 33: 1–23.

¹² Anthony Hugh DeBono published on lung, heart and liver transplantation while at the Department of Surgery, Postgraduate Medical School, Hammersmith Hospital, London, before moving to the University of Wales in 1969. See DeBono A H. (1966) La transplantation cardiopulmonaire totale. *Annales de Chirurgie et Thoracique et Cardio-vasculaire* 5: 243–248. Edward Francis Charles Publius DeBono, a medically trained psychologist, was at Addenbrooke's Hospital, Cambridge, having written papers on blood flow. He lectured in medicine at Cambridge from 1976 to 1983, where he became involved in the promotion of the skills of thinking. He has been Director of the Cognitive Research Trust since 1971. See DeBono E F C P. (1967) *The Use of Lateral Thinking*. London: Cape. Victor Joseph DeBono was in general practice in Leicester.

mention that the thing that fired me off in the first place was Russell Brock having a go at a dog transplant.¹³

Now it came to getting donors and I started a search for how one would get donors, based partly on the experience of the kidney people, and partly on our own views.¹⁴ One of the things which concerned me a great deal was that Professor Ian Aird had sought publicity at the Hammersmith Hospital over the Siamese twins cases, and having sought publicity, it seemed to me that journalists could find lots of plums ripe for picking if they turned the lenses on the medical scene practically anywhere.¹⁵ And I thought we should prepare for transplantation, and so I wrote a jolly, popular book, which was a vehicle for the last chapter which explored the moral, ethical, legal and financial arguments.¹⁶ I wrote it in 1966. It was published, unfortunately, just a couple of days before Louis Washkansky's operation, because there had been a strike at the printers in Italy. I had a patient in the National Heart Hospital, called Bill Bradley, whom Dr Lockey and others here will know, who had watched a whole series of dog heart–lung transplants and had decided it was time he had a set.¹⁷ He was

¹³ Cass M H, Brock R. (1959) Heart excision and replacement. *Guy's Hospital Reports* 108: 285–290. For a review of the field, see Cooper D K C. (1968) Experimental development of cardiac transplantation. *British Medical Journal* iv: 174–181.

¹⁴ On 29 May 1968 the Joint Cardiac Transplant Committee of St Mary's, Guy's and the National Heart Hospital, chaired by Dr James Mowbray, received reports on the criteria for patients for the recipient pool and on the organization of the National Tissue Service. The Middlesex Hospital also had a Feasibility of Transplants Committee, which had been established by the Medical Committee. In 1969 the National Tissue Typing Reference Laboratory was established at the South West Regional Transfusion Centre, Southmead, Bristol, directed by Dr Geoffrey Tovey. The procedures were similar to those described in Buxton M, Acheson R, Caine N, Gibson S, O'Brien B. (1985) *Costs and Benefits of the Heart Transplant Programmes at Harefield and Papworth Hospitals*. Research Report no. 12. London: HMSO.

¹⁵ Professor Ian Aird FRCS (1905–1962) was Professor of Surgery and Director of the Surgical Unit at the Postgraduate Medical School, Hammersmith Hospital, London, from 1946 until his sudden death in 1962. Aird I. (1954) The conjoined twins of Kano. *British Medical Journal* i: 831–837. The publicity took place in December 1953. See Aird I. (1954) Correspondence: Press Publicity. *British Medical Journal* i: 153.

¹⁶ Longmore D. (1968) *Spare Part Surgery: The surgical practice of the future*. London: Aldus Books.

¹⁷ Bill Bradley was 55 years old when he died, having waited seven years for a heart and lung transplant. Farr D. (1968) The man who ran out of time. *The People* (10 November 1968). Professor Donald Longmore wrote: 'Bill Bradley did appear on television with me. He had become a close friend after spending many days with us in the dog laboratory, sometimes accompanied by his wife. I came to know Bill because he received one of the first pacemakers made by Adrian Kantrowitz from New York. It was implanted properly by Professor John Kinmouth at St Thomas's but it never worked. Peter Stiles, the then Chief Technician in the electronics laboratory at St Thomas' Hospital, made a number of pacemakers which worked despite the problem of potting the electronics in a satisfactory manner in Araldite. I implanted one of Stiles's pacemakers in Bradley. ...The programme was "Barnard faces his critics". There was a long televised debate, including Dr Donald Gould who I believe was not a doctor and Malcolm Mugeridge, both of whom were eloquent in their opposition to the procedure. The BBC

admitted to the Heart Hospital, into one of Donald's [Ross] beds, and a few days later a committee headed by the Chairman of the Medical Committee, Dr Graham Hayward,¹⁸ and a number of other people, who I felt should have known better, asked me if I could spare them five minutes. I was faced with an ultimatum which was: that you have nothing to do with this disreputable heart transplant business, you'll bring the hospital into disrepute and if you don't promise not to carry on with your research and not to go on in this area, we will materially damage your career. I didn't, and they did.

I drove many thousands of miles round casualty departments with a radio-telephone system, trying to find how we would get donors and a rabbi, Rabbi Newman, whom I was on a debate with, said, 'Donald, the only way you will ever get donors is to recruit religious organizations'. Now Fred West [who became the first recipient] was a devout Catholic.¹⁹ So I went to the Catholic establishment, and hunted around and found a number of priests who were very interested in supporting us, and following that Edward Raftery at King's College Hospital found us Patrick Ryan, who was a potential donor, a Catholic, and the same relatively rare blood group as Fred West. This was particularly poignant, because Patrick Ryan was a building worker and his job was to lay concrete slabs between beams put down by his chums, and his chums had laid the beams too wide, and when poor Patrick threw down the concrete slab and lay on top of it, it disappeared down between the beams two floors [below] and cut off the top of his head. Although he had a beating heart, there was absolutely no question that this was a brain-dead person, because he didn't have a brain. Now while we were bringing the donor to the National Heart Hospital, regrettably, one of our colleagues alerted the press. We know who it was, and by the time we got the donor to the hospital the press were outside the hospital. I will just finish the donor story quickly, because there's only one minute left. Very briefly, we were

pursued their usual policy of giving equal weight to the scientists and doctors who knew what they were talking about and to every "fringe nutter". Just as the debate was to draw to a close I wheeled Bradley on to the stage and he made the following statement: "It is all very well for you people to talk about theoretical objections to heart transplantation. I am dying and I want one." Letter

to Dr Tilli Tansey, 30 March 1999. Dr Donald Gould qualified at St Thomas's in 1942 and was a medical journalist for the *New Scientist* from 1966 to 1969 and the *New Statesman* from 1966 to 1978.

¹⁸ Dr Graham W Hayward FRCP (1911–1976) was a consultant physician at the National Heart Hospital and its dean from 1948 to 1961.

¹⁹ Father James McGettrick, a Camberwell Roman Catholic priest, was also chaplain to King's College Hospital, Denmark Hill, and had known Mr West for two months prior to the transplant. See Delin J. (1968) Pop music in operation. *Sunday Telegraph* (5 May 1968). Father McGettrick administered the final rites to Patrick Ryan at King's College Hospital. Wilkinson J, Steemson M, Smith C, Cheesewright A. (1968) A priest explains: I have to rely on the medical men. *Daily Express* (6 May 1968).

horrified because we had asked the press to leave the donor's family alone, his wife was having a miscarriage. Two journalists broke into his in-laws' house, stole the wedding photograph off the mantelpiece and had a fight over it, and the only other important bit about the donor story here – Keith and Donald [Ross] took the heart out, having waited for it to stop – was a very nasty coroner's inquest which was stirred up by the press. And if I hadn't taken the skull and photographs with me, we would have been in very serious difficulties.

Treasure: I have the details of that inquest here and your statement to them in the *British Medical Journal* of that year.²⁰ We will come back to that. I wanted to pause there because I want Sir Keith, the surgeon who had to perform this very dramatic procedure of taking out a heart, to tell us about the donor operation.

Sir Keith Ross:²¹ Would you allow me first of all to go back just a little in time, because Shumway's name has been mentioned already and just to put one's awareness of heart transplantation into perspective as far as I was concerned. I was fortunate enough to work with Dr Frank Gerbode in San Francisco, in the same laboratory as Norman Shumway, in 1959. The main effect of this was that when I got there at 8.00, he had already been working for about two hours and Dr Ray Stofer, the veterinarian who ran their pump oxygenator, had already bled donor dogs to prime the machine.²² Richard Lower and Norman Shumway, when I first arrived there, were transplanting valves into various parts of the circulatory system, the aortic valve was being transplanted either into the descending aorta or into the mitral position and, by the time I left in December 1959, they had started doing the first orthotopic heart transplants in dogs. One was very much aware, not only of what was going on in the world of heart transplantation experiments at that time, but also the personalities of the people involved with that effort.

So far as the personal recollections of the first transplant at the National Heart Hospital are concerned, again to fill in the background, I had been appointed as Consultant Surgeon there in September 1967 and had therefore only been on the staff for about two-and-a-half months when the first rumblings, if you like, of the possibility of a heart–lung transplant were produced. I was in a very difficult and

²⁰ Anon. (1968) Medical News: Inquest on heart donor. *British Medical Journal* ii: 569. See page 32–33 below.

²¹ Sir Keith Ross Bt FRCS (1927–2003) was Consultant Surgeon at the National Heart Hospital from 1967 to 1972; and Consultant Cardiac Surgeon, Wessex Region, Southampton from 1972 to 1990. He was Senior Registrar at the Middlesex and Harefield Hospitals from 1961 to 1964 and Consultant Surgeon at Harefield from 1964 to 1967. He was President of the Society of Cardiothoracic Surgeons in 1988 and a member of the Council of the Royal College of Surgeons from 1986 to 1994. He chaired the Working Party on Cardiac Transplantation of the Royal College of Surgeons of England, from 1990 to 1992. [updated 19/1/06]

²² Stofer R C. (1968) *A Technic for Extracorporeal Circulation*. Springfield, IL: Charles Thomas.

unsustainable position at that time, and I freely admit that I was at the meeting which Donald [Longmore] described and felt that I personally couldn't cooperate with that particular effort.

So far as the operation on 3 May 1968 was concerned, we had already been to the Veterinary College on two occasions and the entire team had carried out standard experimental heart transplants, I think with reasonable success. They were non-survival acute experiments, which familiarized members of the team with the procedure.²³ On that day, the donor arrived at the hospital at 14.25 and went into ventricular fibrillation in the lift going up to the theatre and the heart was kept going by external cardiac massage. We had twin theatres at the Heart Hospital, and the recipient was in one theatre with Donald [Ross] getting him ready and I had the job of taking the donor heart out. The patient was on the table by 14.35 in the afternoon and a number of observations were made and blood cultures were taken. The ventilator was switched off at 16.09, and by 16.30 all the traces on the various recordings were flat. The ventilator was restarted at 16.38, external cardiac massage was given, the chest was opened, heparin was given, and the heart was actually removed by 17.47; it took 11 minutes to get the heart out. Removing the heart was a novel experience and I saw parts of the intrapericardial anatomy in a novel way. I was relieved to get the donor heart out without damage, which of course would have been a sad thing to do at the beginning of this whole procedure. The time for the insertion of the donor heart, up to the time that the aortic clamp was released, was 48 minutes. The donor heart was not refrigerated in any way, other than being kept in a bowl of cold saline while it was transferred from one theatre to the other and I must say that we were all immensely relieved to see that it was able to beat when the aortic clamp was released. It was an intensely dramatic moment, I think for everybody there, as it became pink and began to beat when the aortic clamp was released. When it did begin to beat the right heart distended and had to be sustained with isoprenaline, but happily there was no leakage from any of the suture lines, not that I can remember anyway, because I was responsible for half of them and Donald [Ross] the other half. We stood opposite each other and did whatever came to hand most easily. The only other thing I would like to say at this stage is that one was aware, very much I think, while this was going on, that this was a historic moment and slightly unreal in the relative calm of the operating theatre at the National Heart Hospital.

²³ In Britain, the conduct and conditions of animal experimentation were and are regulated by the Home Office under the Cruelty to Animals Act 1876, later replaced with the Animals (Scientific Procedures) Act 1986. The Act permitted such acute experiments to be performed by a licensed operator, working on registered premises, animals had to be anaesthetized throughout the procedure, and were not allowed to recover.

Treasure: That's fascinating because there are some of us here who do heart transplants, but there are many who don't, but although Donald Ross very modestly says 'a simple piece of plumbing', the time in which this was performed, and the time to removal of the cross clamp, is actually a very competitive time by any standards and to do it, the first time, to that standard is truly remarkable and I think that must be recognized. Donald Ross, do you want to rejoin the discussion now at this point, or shall we ask an anaesthetist?

Donald Ross: I have been fascinated to hear the story so far [Laughter]. It reminds me of the dramatic occasion when the heart began to beat – we were greatly relieved. At first the heart action was poor until we gave it a stimulant (isoprenaline). We were ignorant about what reaction to expect from the heart, but fortunately, nature took over and the heart action continued satisfactorily.

Treasure: Well, thank you very much. Now, of course, we have tried very hard to track down all the people who I knew were involved and I may have missed some. For all I know, some people have come today who were involved but I don't know who they are – but do please volunteer to speak. Alan Gilston is the one I think we should ask, because he was one of the two anaesthetists present.

Dr Alan Gilston:²⁴ First of all, I have just reminded Donald Longmore that in fact the first transplant was a pig heart transplant in the hospital, and I remember chasing piggy round the corridors of the hospital. I had never anaesthetized a pig before, but that wasn't terribly successful, so we didn't have the press in on that. The first thing I knew about the human heart transplant was I got a red alert signal by phone from Donald Ross and I dashed in and we took the patient to theatre. There were no special anaesthetic problems because, as you know, the question of patients being fit for a general anaesthetic is absolute rubbish and asking a physician about his opinion as to whether a patient is fit for a general anaesthetic is largely a waste of time. There is no such thing as not being fit for a general anaesthetic.²⁵ They may not be fit for the operation, but there is certainly

²⁴ Dr Alan Gilston FRCS FFARCS (1928–2005) was Senior Consultant Anaesthesiologist at the National Heart Hospital from 1967 to 1990. A former president and founder of the World Federation of Societies of Intensive and Critical Care Medicine, Secretary-General and initiator of the First World Congress on Intensive Care in 1974, and Chairman and founder of the Intensive Care Society, who gave the first Gilston Lecture, and Silver Medallist of the Society. [updated 19/1/06]

²⁵ Dr Alan Gilston wrote: 'Mechanical ventilation played, and I believe continues to play, a vital role in saving patients with a respiratory problem after cardiac surgery. But it was severely opposed by many surgeons, and this is so even today. Many years ago I published a formula: "Sick patients often need mechanical ventilation for respiratory failure. Sick patients often die. Ergo (in the surgeon's view) ventilators kill patients". I have suffered grave professional consequences from one case where a surgeon refused to allow mechanical ventilation in a patient who could have been saved. The trouble is that whilst lip service is paid to other members of the team, in fact the surgeon takes all the credit. The Brompton Hospital some years ago instituted a

no such thing as not being fit for the anaesthetic. After the operation we had no resident anaesthetist at that time, so I slept on the trolley next to the patient in the operating theatre and unfortunately in the middle of the night the central venous line came out and we had to put another one in, and I was worried in case I was the first anaesthetist to kill a heart transplant patient. I wasn't sure what anaesthesia for heart transplant patients who had had the operation was, but eventually we did it [insertion of central venous line] under local.

Another point is that my Registrar, Dr Ann Naylor, told me afterwards she was very upset after the operation because here she had, as it were, a live human being and then they snatched his heart away and although he was a donor and it was all done ethically and properly, she told me afterwards that she was very upset about it.

Treasure: Thank you very much. Now to move into a post-operative phase, you have got this chart which you only have to look at to realize the labour involved in minute by minute, hour by hour, day by day, charting the progress of this patient and this one includes some chemistry and the immunosuppressant drugs and so on. Simon Joseph was the resident at the Heart Hospital at the time, a mere boy then no doubt, an SHO [Senior House Officer]. Can you tell us about all this, Simon.

Dr Simon Joseph:²⁶ Well I can try. I feel a mere boy now actually with the assembled company, although I must say it's very pleasant to meet everybody again. I think you [Donald Ross] launched me on my career. I actually started at the [National] Heart Hospital at the same time as Keith [Ross]. In fact, I remember walking into the Heart Hospital, Uncle Tom was coming out and he held the door open for me. I don't know whether it was his last day.

Treasure: We should say that Uncle Tom was Sir Thomas Holmes Sellors, always known as Uncle Tom.²⁷

policy whereby the surgeon loses charge of critically ill patients to intensivists. There is now an intensivist with an outstanding international reputation in charge of the Intensive Care Unit.' Letter to Dr Daphne Christie, 14 November 1997.

²⁶ Dr Simon Joseph FRCP (b. 1940) has been Consultant Cardiologist at Mayday University Hospital, Croydon, since 1979. He was Resident Surgical Officer in the ITU after the first heart transplant in the UK in 1968. We are grateful to him for making the chart available to the Witness Seminar, which shows some of the post-operative clinical details and for giving us permission to reproduce it here on pages 14–15.

²⁷ See biographical note, op. cit. note 10 above.

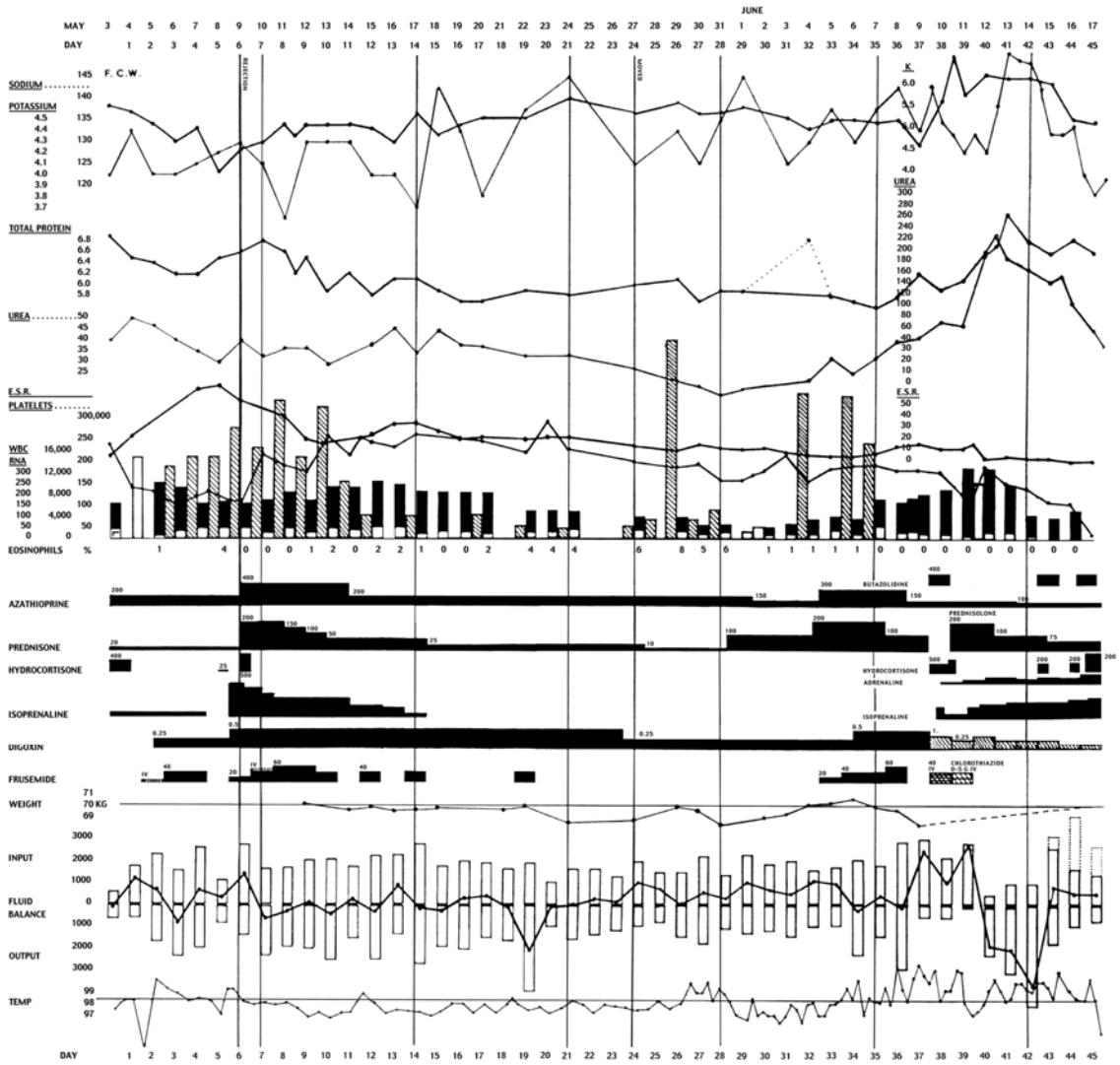
Joseph: I don't actually know whether it was his last day or whether he was just paying a visit, but it stuck in my mind. I was obviously proud to be associated with this. I cannot recall at the time of the surgery where I was and what I was doing, but being junior, I was not allowed access to the patient for quite a few days. The thing that strikes me now, looking back on it, was the relative freedom that everybody had to do it. If one was making a world-shaking advance now, one would probably have to apply to statutory bodies for permission, acquire the funds and get it approved by many committees. I imagine that it would be much more difficult today. I think my main contribution was artistic, in keeping a record of what happened! The patient was kept in theatre for about two weeks. About half-way through the chart you will see a vertical line, which says 'moved', when he was moved from theatre to recovery.

One thing that concerned everybody most at the time was trying to pin-point episodes of rejection. Another thing that strikes me now is the relative paucity of drugs that we had available at the time. As you say, he came off bypass on isoprenaline, and isoprenaline was really the only sympathomimetic drug we had, apart from adrenaline. It was used in quite large doses early on. The first vertical line represents what was thought to be an episode of rejection which was associated with a fever (at the bottom of the chart) and a fall in platelet count. The doses of prednisone and the azathioprine, which were the only drugs available, were intensified considerably. They were reintroduced at various points in his course when further episodes of rejection were diagnosed. On this chart [*see pages 14–15*] I have documented something called 'RNA', I cannot, now, remember exactly what measurement this was, but it was used as an assessment of rejection.²⁸ Another thing that struck me (on reading through the longest clinical

²⁸ Professor James Mowbray wrote: 'In 1967 a research worker and PhD student in the Department of Surgery at Guy's, Joan Parker, developed this test. Although she was a graduate student at Guy's she had asked me to be her supervisor, and her other connection with cardiac transplantation was that she is a cousin of Donald Ross! The work she has done and which is the basis of her PhD thesis relates to an observation originally that during rejection episodes in renal transplantation there was an increase in RNA synthesis in a subpopulation of blood mononuclear cells. This became, in its time, quite a useful adjunct to other ways of detecting rejection episodes in renal allografts, and thus unsurprisingly Donald Ross suggested looking at it in the cardiac allograft patients. It correlated well with other evidence of impending rejection episodes, and was one of the criteria used to decide to treat a cardiac rejection episode by increasing the doses of immunosuppression, particularly of corticosteroids. Subsequent to this, in the first two patients treated Joan finished her work, and at the last moment showed, with the help of Dr Bessis in Paris, that the high RNA synthesizing peripheral blood population was not lymphoid, but was in fact composed of promyelocytes of myeloid origin. Some very pretty electron micrographs of these promyelocytes were obtained from the blood of one patient with a cardiac rejection episode. The reason for this appearance of promyelocytes in the blood from the bone marrow at this time remains a mystery.' Letter to Mrs Lois Reynolds, 19 May 1999. See Parker J R. (1969) The effect of immunization on RNA synthesis in peripheral blood leukocytes. PhD thesis, University of London.

Post operative data of heart transplant recipient, Mr FW, aged 45 from day zero (3 May 1968) to day 45, showing **blood chemistry** (sodium, potassium, total protein and urea), **haematology** (WBC, white blood cell count, ESR, erythrocyte sedimentation rate, platelets and eosinophil count), **medication** (azathioprine, prednisolone, hydrocortisone, isoprenaline, adrenaline, digoxin and frusemide), **fluid balance**, **weight**, and **temperature**. Haemodynamics were not recorded on this chart, which was mainly used to record treatment and other features which might assist the diagnosis of infection and rejection including fluid balance, renal function and 'RNA' [*see footnote 28*]. On day 6 there is an episode of rejection with a fall in cardiac output, a fever and a low platelet count; treatment with azathioprine and prednisolone was increased. On the following day he developed pulmonary lesions and chest pain which may have been the first signs of pulmonary infarction and there were signs of right heart failure subsequently. There were episodes of fever on day 12 and 18 but no clear evidence of infection or rejection. He was transferred to the ward on day 24. There were further episodes of rejection on day 26 (with fatigue, pyrexia and reduced platelets) and day 33 with persisting heart failure subsequently and evidence of pulmonary infarction and infection; medication was increased. There were further haemodynamic deterioration on day 36 and haemodynamic collapse on day 38 with progressive deterioration subsequently. *Dr Simon Joseph*

Early Heart Transplant Surgery in the UK



summary I ever wrote, a copy of which I have just given to Donald Ross), was the fact that there were episodes in which we thought he had pulmonary infarction. One was fairly early, around six days, where he had pulmonary lesions on chest X-ray; these lesions resolved and he was not treated specifically for them. Much later, at about 36 days, he developed further pulmonary lesions and pulmonary emboli were considered likely. At this point he was then heparinized. I do not have an autopsy report, but I recall that his downfall was in fact pulmonary emboli and pulmonary infarction. Looking back on it now, it seems a shame that this wasn't perhaps picked up and acted on earlier. There was certainly right heart failure with a raised venous pressure, which was treated, but the underlying pathology was not really recognized. I also remember quite clearly at around eight to ten days the patient became clinically very depressed. I developed a working relationship with him at this time which was special. Around 25 days was when he was at his best, he was very happy and the depression largely lifted.

Booth: For an ignoramus, the chart is extremely complicated and difficult. I presume you recorded the pulse rate?

Joseph: Yes, haemodynamic measurements were recorded separately by somebody else and I do not think they survived. As I recall we had an enormous chart with pulse and blood pressure. Jane [Somerville] may perhaps remember more than I, but it did not feature on this chart.

Dr Jane Somerville:²⁹ Donald [Ross] said to me, I don't know, about lunchtime on that day, 'What are you doing tonight, Jane' and I said, 'Why do you want to know?' So he said, 'You are going to be the physician to the first transplant', so that's how I came into it. I at the time was a senior lecturer without consultant status although I think I thought, I sort of pretended, I had it. I don't think we got it automatically then. So I found myself physician to the first transplant and I think this was because I spent a lot of time with the cardiac surgeons at the time. We spent a lot of time in theatre and a lot of time with them. There was a lot of new valve work coming, so they were used to a not very tame physician, but anyhow an interested one. Two things struck me that night. I think I was in the gallery of the theatre, the absolute horror of seeing a live patient without a heart in their chest and I can remember it to this day and I had exactly the same

²⁹ Dr Jane Somerville FRCP (b. 1933) was Honorary Consultant Physician from 1967 to 1974 and Consultant Physician for congenital heart diseases from 1974 at the National Heart Hospital, which later joined with the Brompton Hospital from 1990 as the Royal Brompton and National Heart Hospital, until her retirement in 1999. She established the first adolescent cardiac unit in the world in 1975 and rebuilt the Grown-up Congenital Heart (GUCH) Unit at the Royal Brompton Hospital, which in 1997 was named the Jane Somerville GUCH Unit. See Oh W, Hickman R, Emanuel R, McDonald L, Somerville J, Ross D, Ross K, Gonzalez-Lavin L. (1973) Heart valve surgery in 114 patients over the age of 60. *British Heart Journal* 35: 174–180.

feeling, because I was on the donor removal of the heart at Guy's.³⁰ It's true, and I had the same feeling, it was almost a revulsion. So having got over that and the joy of the beating heart, and we were really very elated late into the night, and the House Governor, Mr [R J] Denney, stayed on with us, I think he didn't know what was going to happen next, but while all this was going on, and we didn't know what was going on outside, there was accumulating outside the National Heart Hospital, which is in a little narrow street as you know, this massive amount of media, something that we had never encountered in our lives. Mr Denney said to us, 'I think you'd better come outside and speak to the press' and I don't know what time it was, Donald [Longmore] will know, but we went out and there were arc lights, so you couldn't quite see how many people were there, and the whole thing looked like a royal wedding being watched, it was unbelievable when you saw the masses there, and we found ourselves on live television.³¹ It was quite terrifying and from then on, for the next six or seven weeks, we had a rotten time with the press one way and another, part of it being that we didn't know how to cope with them.

Back to the medicine. Simon [Joseph] has given you a very good appraisal, but one of the things I remember about this period is that we used to have these hour-long conferences, or longer, twice a day, interspersed with a lot of ringing up of Chris Barnard, which was always fun, and you know he would say, 'Go with it, boy' and give us a lot of odd advice, and we were looking for globulin and all sorts of things, but certainly the episodes that Simon mentions were very dominant. Is James Mowbray here? [Treasure: No. Apologies, he had to go to Canada.] James Mowbray³² liked talking about everything and in great detail and he knew much more about clinical immunology than any of us understood, and he was responsible for these hugely long conferences that went on. Anyway, everybody was interested in suppressing the patient's immune response, but in actual fact it was quite obvious this chap was throwing off pulmonary emboli, and given anything but a transplant, we could have made the diagnosis and indeed we did press to have him on heavy heparin doses. I think cardiologically and

³⁰ The third transplant was performed at Guy's Hospital on 16 May 1969.

³¹ Express Staff Reporters. (1968) Heart Transplant – The British Team. *Daily Express* (4 May 1968). The team of 18 came to stand on the steps of the National Heart Hospital, London, at 22.10 on Friday, 3 May 1968, following the operation, which ended at 21.30.

³² Professor James F Mowbray FRCP (b. 1930) was Professor of Immunopathology at St Mary's Hospital Medical School from 1974 to 1995, now Emeritus. He was unable to attend the Witness Seminar. See Pletka P, Kenyon J R, Snell M, Cohen S L, Owen K, Mowbray J F, Hulme B, Thompson A E, Porter K A, Leigh D A, Peart W S. (1969) Cadaveric renal transplantation: An analysis of 65 cases. *Lancet* i: 1–5. O'Connell T X, Gonzalez-Lavin L, Milton J D, Mowbray J F. (1974) Improved survival of canine heterotopic cardiac transplants without immunosuppression. *Journal of Thoracic and Cardiovascular Surgery* 67: 459–465.

medically you could see this was what was happening, but one got completely distracted by the fact that this was a transplant.³³

Treasure: Where I would like to move to now is that very soon after this the second transplant was done at Guy's. Donald Ross was again the surgeon. The task that was performed at the first transplant by Simon Joseph, was undertaken by his junior staff. Tony Dyde and Barry Ross were the two I know were involved. Tony Dyde sends his apologies.³⁴ Barry Ross, what are your recollections?

Donald Ross: That was the third transplant.³⁵

Mr Barry Ross:³⁶ Of course, *el supremo* [Donald Ross] is right, Guy's was the third transplant. Can I just put this in perspective. I first met Alan Gilston in Ipswich in 1963 when he was doing a locum and I was Registrar to a lovely surgeon but he was rather slow and when Alan was asked what time the list was going to finish he said, 'Bugger the time, I am worried about the date!' I think again, to put this in perspective, I don't know if any of you have seen the film of how to do a brilliant prostatectomy – you see this perfect operation with no blood and the catheter is put into the bladder afterwards and washed out and this beautiful clear urine comes out and then they stop the film and say, 'And now we'll show you what really happened' and, of course, it's a shambles, there's blood all over the place, clot retention and it really is anything but a perfect operation. I was involved in the first lung transplant that we did at Guy's, which I think is interesting – to put this into perspective – because this was earlier in the summer of 1969, when we did a single lung transplant, probably as Simon [Joseph] has said, you wouldn't be able to do these things now without ethical permission, but I think we had a patient in end-stage emphysema and it was rather a good thing to do a lung transplant. We had a donor and we popped in a single lung one evening, and this was the most amazing concept of somebody with a transplanted

³³ Mr Frederick West, aged 45, died on 17 June 1968, 45 days after the cardiac allograft.

³⁴ Mr Tony Dyde FRCS (b. 1935) was Consultant Cardiac Surgeon at the West Midlands Regional Cardiothoracic Unit, Walsgrave Hospital, in Coventry from 1972 to 1997, now retired. Mr Dyde wrote: 'Strange as it may seem, my notes and slides were confiscated at Karachi airport and never returned to me.' Letter to Professor Tom Treasure, 11 November 1996.

³⁵ The second transplant was performed at the National Heart Hospital by the same team on 26 July 1968. The recipient was Mr Gordon Forde, 48, and the donor was Mr Derek Birkbeck, 32, who died in a car accident.

³⁶ Mr Barry Ross FRCS (b. 1934) was Consultant Thoracic Surgeon with the East Anglian Regional Health Authority, now retired. He was Senior Registrar in Thoracic Surgery at Guy's Hospital from 1967 to 1970.

lung, with gross emphysema in the other lung and we ended up with rejection, and the typical non-compliance of the transplanted lung which was rejecting. Unfortunately I don't have the slide, I would love to show it to you, of this patient just before he died, being ventilated through a double lumen tube, two ventilators ventilating asynchronously each lung, one pressure-cycled, the other volume-cycled, in order to try and overcome this desperate problem. Well, this chap survived a week, and then a few weeks later, in May 1969 we did a heart transplant at Guy's.

Fortunately, I was on holiday when it was done. David Carnegie³⁷ was the anaesthetist at the Guy's transplant, and he tells me that it was done on a Friday night and I returned from holiday on Sunday when the drama was all over, but having to pick up the pieces, rather as Simon [Joseph] did, as the junior boy. I have lasting recollections of the following three months, which was probably the hardest work that I have ever done, before or since, of looking after this patient. And I think the first of the three recollections that I will share with you just for the moment is that I found that you can never manage a patient by committee. We had a very strong team at Guy's of Maurice Lessof, whom I see over there, Dick Batchelor looking after immunology, and Dennis Deuchar our cardiologist, and they would make very sound and wise pronouncements, and then about 16.00 the National Heart team would swan in, in the form of Jane [Somerville], James Mowbray and a couple of others, and produce diametrically opposite views, and this became extremely difficult and we actually had to institute a book which, I don't know what's happened to this book, but it would be very valuable reading now. Tony Dyde, who bore the brunt of this, insisted that anybody who attended the patient recorded their thoughts and their dictats, so that when Donald [Ross] came in, and would then say, 'What the bloody hell have you done this for?' we could say, 'Well Jane Somerville told us to do it, here's her signature over this order', and it really did become extremely difficult. The second lasting memory that I have is of the donor's relative, and I think it was her father, who insisted on seeing the embodiment of his daughter in this chap Hendrick,³⁸ and he made a tremendous scene and was, eventually, after a big fight, ushered

³⁷ Dr David Carnegie (b. 1917) is Consultant Anaesthetist Emeritus at Guy's Hospital, London. He started cardiac anaesthesia with Russell (later Lord) Brock and did his first mitral valvotomies in 1948, and continued at Guy's Hospital with Donald Ross and Alan Yates until 1980.

³⁸ Mr Charles Hendrick, 59, was the recipient of a heart transplanted at Guy's Hospital on 16 May 1969. Anon. (1969) Hendrick has fungus infection. *Daily Telegraph* (19 August 1969). Mr Tony Dyde wrote: 'He [Hendrick] was a hypertensive with a failed LV [left ventricle] who received the small heart of a young girl. I distinctly remember that for most of his few weeks' survival he was well perfused with a BP [blood pressure] below 100, which I thought was rather odd....I remember being very impressed with the power of steroids, because at his PM [*post mortem*] nothing had healed. The suture lines were exactly as they were when he left the theatre.' Letter to Professor Tom Treasure, 11 November 1996.

into the room, to view this poor patient in whose body his daughter's heart lay. Now this was a pretty emotional time. I don't know if you remember that, Donald [Ross]? The third thing that sticks in my mind is that we needed PR. Everyone has talked about the management of the press, and a fellow who came hot-foot from the BALPA [British Air Line Pilots' Association] dispute with the Government over the airline pilots' pay and Mr Norman Tebbit (now Lord Tebbit), was a chap called John Gorst.³⁹ Now whether he offered his services to us or whether Donald hired him, I can't actually remember, but he took on the PR. I have a word for him, which actually begins with PR and ends in CK, but he was actually a pain in the neck, but it was a very, very difficult three months, certainly for a member of the junior staff. We haven't, as far as I know, got any of the scientific data here, but all I can say is that at that time without the Shumway regime and the sort of things that Terence English will have introduced later, which would have made the management of a transplant patient so much easier, we really were thrashing about in the dark. Hendrick lived for about three months. Alan Yates was sort of coordinating the surgical element and was a very wise counsel from the Guy's point of view and Alan and I were in at the last cardiac massage just before he died. So he died, I think, in the September of that year.

Treasure: Thank you very much. I don't want to forget the anaesthetists, because we have got some key anaesthetists here, but first on the medical support side Dr Eunice Lockey was at the National Heart Hospital and I am glad to see here Professor Lessof. Would either of you like to tell us your memories of these aspects.

Professor Maurice Lessof:⁴⁰ My main impression was how far ahead the surgeons were, compared with the immunologists. It was embarrassing that, for instance, when Donald [Ross] pioneered the transplantation of cadaver aortic valves and they did so well, we started off trying to immunosuppress the patients without realizing that all you had to do was treat the homografts like bits of leather and leave them alone. To some extent we did more harm to the first few patients than any good. As far as Donald's [Ross] heart transplant efforts here were concerned, I think that he would have started much sooner if it wasn't that the people on the medical side were saying, 'No, no, Donald, we are not ready yet.' Indeed I think

³⁹ Sir John Gorst (b. 1928) was public relations adviser to Guy's Hospital from 1968 to 1974. He had been Advertising and Public Relations Manager of Pye Ltd from 1953 to 1963 before starting his own consultancy for trade union and public affairs, John Gorst & Associates, in 1964. He was MP (Con) for Hendon North from 1970 to 1997.

⁴⁰ Professor Maurice H Lessof FRCP (b. 1924) was Consultant Physician and Clinical Immunologist to Guy's Hospital, later Professor of Medicine to Guy's from 1971 (later the United Medical and Dental Schools of Guy's and St Thomas's Hospitals) until his retirement in 1989, now Professor Emeritus.

he probably would have gone ahead before Barnard if it hadn't been for that. Our efforts were not very well coordinated and by modern standards not very scientific – and if they were not the cause of the problems, they at least did not solve them.

Dr Eunice Lockey:⁴¹ I don't have a great deal to add. Jane talked about being appalled at seeing a live patient without a heart. My greatly respected colleague, Reggie Hudson,⁴² was very opposed to heart transplantation at that time and upset that it was not a whole person [the donor] in his *post mortem* room.

I think we kept Mr West so long in theatre because we had very few single rooms and we were very concerned about infection. People hesitate before going into an operating theatre, because they have got to get undressed and redressed and put on hats and overshoes. You can keep a good deal more control over who is going in and out. Movement greatly helps in the spread of bacteria. We learnt this particularly when a large chunk of ceiling plaster fell off in our operating theatre suite; not at that time, but earlier, and the theatres had to be closed whilst they were replastered. Donald Longmore created a plastic operating tent which was put up in the ITU.⁴³ This sounds like a joke, but you could actually sterilize the area, and we did open heart surgery there with no problems.

The first day was like a circus, people we didn't know existed arrived at the theatre to see the performance, so to speak, and the bacterial fall-out was incredible. After that Sister Curry (the theatre superintendent) and I stationed ourselves at the entrance and if we didn't recollect seeing someone before, we asked them what their function was. The fall-out of bacteria went down to very little. But there were always plenty of people with Mr West. He wasn't on his own by any means.

Treasure: I think we ought to hear from the anaesthetists. They always tend to be forgotten by surgeons don't they? But in the whole of our work in

⁴¹ Dr Eunice Lockey (b. 1925) was a Consultant Clinical Pathologist with particular interest in open heart surgery and intensive care work, and a consultant at the National Heart Hospital from 1963 to 1974.

⁴² Professor Reginald Hudson (1910–1992) was cardiovascular pathologist at the National Heart Hospital from his appointment in 1948 and Professor of Pathology at the Institute of Cardiology, University of London (associated with the British Postgraduate Medical Federation and later the National Heart Hospital, merged in 1972 with the Institute of Diseases of the Chest to form the Cardiothoracic Institute, renamed the National Heart and Lung Institute, and merged with Imperial College of Science, Technology and Medicine as part of its new Biomedical Science Faculty in 1995) from 1966 until his retirement in 1971, then Emeritus. See Hudson R E B. (1965–1970) *Cardiovascular Pathology*. 3 vols. Baltimore, MD: Williams & Wilkins.

⁴³ Anon. (1965) Hospital shuts operating theatres. *The Times* (2 April 1965).

cardiothoracic surgery, of course, they are central and their willingness to cooperate with some of the things that we get up to is the only reason, of course, that we can go ahead. Professor John Bunker is here, and although he wasn't part of the London work, he was with Norman Shumway and his written recollections of it are fascinating and very entertaining. Professor Bunker, Shumway's role in all this has been mentioned, and the fact that he got Christiaan Barnard started, and was behind all this thinking, has been referred to by Donald Ross. Can you tell us a bit about it?

Professor John Bunker:⁴⁴ The first heart transplant at Stanford was as interesting for us as yours was for you a few months later. Shumway had completed ten years of research in animals by the time that Christiaan Barnard visited for two months at Stanford and then went home to perform the world's first human transplant. If Shumway complained, I'm sure that I would have heard, and he never did. I don't think he resented the fact that Barnard had one-upped him, but rather that he found that Barnard's transplant had opened the doors, because we were in a very difficult medico-legal impasse at that time.

Shumway had made extensive preparation in the surgical laboratory, but there was little warning, except to the cardiologists, that a transplant was about to occur. I do know that he hadn't consulted us in anaesthesia, nor was there warning to the blood bank or to the haematologists. In the event there were 288 transfusions during the surgery and the three following days that the patient lived, and the haematologists found themselves confronted with haematological problems entirely new to them. I had great difficulty in recruiting my colleagues in anaesthesia to participate. There were only two of us willing to have anything to do with the transplant, because we had been warned by the local district attorney that we could expect to be indicted for murder. I assigned myself to provide support to the donor and Dr Charles Witcher was the anaesthetist for the recipient.⁴⁵

At that time brain death had not been established as a legal basis for organ transplantation. The local coroner was not pleased that the heart was removed before he could carry out an autopsy. He said, afterwards, 'When I do an autopsy,

⁴⁴ Professor John Bunker (b. 1920) was Professor of Anaesthesia at Stanford University from 1960 to 1989, now Emeritus, and Visiting Professor at the Department of Epidemiology and Public Health at University College Hospital Medical School since 1990. See Bunker J. (1972) *The Anesthesiologist and the Surgeon*. Boston, MA: Little Brown, especially chapter 8, 'Transplanting the heart at Stanford: Shumway and the anesthesiologists', 123–138.

⁴⁵ Mr Mike Kasperak, aged 54, received the heart of Mrs Virginia White, aged 43, who had a massive subarachnoid haemorrhage, on 6 January 1968. The blood bank provided 288 units of blood in the two weeks until his death. The definition of death depended on whether the heart could be revived. op. cit. note 44 above, 126–128. Mr Kasperak died after 15 days.

I don't want anyone fiddling with my bodies.'⁴⁶ Shumway was not deterred by the possibility that he might be indicted for murder, nor was I. So we went ahead, willy nilly, and fortunately the district attorney for the State of California took a much more realistic view of the matter. There was some talk about 'Why weren't the lawyers there to set the guidelines that would have protected us in advance?' The lawyers responded that 'You in medicine have to establish your procedures and we will try to determine how to legalize them afterwards.'⁴⁷

So that's what happened. I do want to add that the role of the cardiologists was central to the subsequent extraordinarily good record at Stanford. At the end of the first four years, Shumway's one-year survival rate was 40 per cent, as opposed to 15 per cent worldwide. Shumway's technical accomplishment was remarkable, but the cardiologists, John Schroeder and Don Harrison, deserve equal credit for their day-to-day care in the post-operative days and months.⁴⁸

Treasure: The Guy's anaesthetists of the time are also here, two of them – Dr Raymond Vale and Dr Carnegie, whom I remember very well from my days as Houseman.

Dr David Carnegie:⁴⁹ I can give you a bit of information, because I happen to have the original anaesthetic record card for Donald Ross's transplant at Guy's; also, I can tell you something about the donor. The operation took place on Friday, 16 May 1969. On the Thursday afternoon I was doing the routine cardiac list with Donald [Ross] when a message came through to him saying that there was a possible casualty that could be used as a donor for a heart transplant. The next thing that happened, he asked me if I could go down to Putney Hospital because a nurse had been injured in a motorcycle accident two days previously and they thought she might be a suitable donor. I went down in the ambulance, found her on a ventilator, took her off, ventilated her by hand, and brought her back on Thursday evening to Guy's. The following morning she had an EEG, was considered brain-dead and therefore suitable as a donor. So that afternoon at 17.20, we started the operation and I thought a heart transplant would go on for about eight or ten hours, but I discovered it was a much quicker

⁴⁶ op. cit. note 44 above, 130.

⁴⁷ 'It would appear to me that due to the uniqueness of such operational procedures and the lack of the ability of the law to anticipate problems until they arise that this entire matter requires the utmost cooperation and understanding by all concerned.' District Attorney, Santa Clara County, name not given. *San Jose Mercury*, 27 August 1968. op. cit. note 44 above, quote on page 131.

⁴⁸ Stinson E B, Dong E Jr, Schroeder J S, Harrison D C, Shumway N E. (1968) Initial clinical experience with heart transplantation. *American Journal of Cardiology* 22: 791–803.

⁴⁹ See biographical note, op. cit. note 37 above.

operation than a lot of the heart valves that we dealt with. We started the operation at 17.20, at 18.15 they were on to bypass, at 19.30 we were off bypass and the patient was back in the intensive care unit by 21.30, in very good condition. I think it was the fact that Donald [Ross] had the vast experience of two cardiac transplants, that when he came to do the one in which I was involved, it was all extremely quick and much easier than a lot of the other cardiac surgery.

Jane Somerville: I would just like to say that John Gorst⁵⁰ came to our rescue when we made such a complete mess up of publicity soon after, when we were quite delighted with ourselves and had a press conference and appeared waving union jacks or something and that was not thought very good.⁵¹ I don't know what we said, there must be a record somewhere, but we were in the Heart Hospital and we appeared at the request of the House Governor and it was all arranged and the press were there and there were microphones and then sometime after that. John Gorst sort of produced himself and said, 'You chaps don't know how to handle publicity, I will help you'. He came in with the first transplant and then he did everything after that. So if at Guy's, number three, four, or whatever it is down the line, by then John Gorst was a veritable professor of handling transplant PR – I think you can become a professor with as little as three cases.

Donald Ross: It was a very unusual thing – public relations in relation to surgery – and we were in a mess with our first transplant in relation to the press particularly. We got a lot of hostile press, a lot of hostile telegrams and letters threatening to kill me and so on. So I think we needed a good public relations person and John Gorst, who is now Sir John Gorst, appeared. I don't know where he came from as a matter of fact, but he was very welcome and he guided us from that time on through all the three transplants. I must say, I know my colleague on my left [Barry Ross] doesn't share my view, but I welcomed him then, and would welcome him again.

Treasure: Donald Ross, thank you, that's very helpful. Just for the record, I have been through all the correspondence columns of the *British Medical Journal*, which do include some criticism, but also include a great deal of support.

⁵⁰ See biographical note, op. cit. note 39 above.

⁵¹ Professor Hedley Atkins, President of the Royal College of Surgeons, in a letter to *The Times* on 19 June 1968, thought it would be unwise for Parliament to ban the operations.

As Jane [and] Donald Ross say, there was a certain amount of flak being thrown around, but there was support.

Joseph: May I just say that one of the reasons for the flag raising was that it got mixed up with the 'I'm Backing Britain' campaign, which was in full swing at the time. I cannot remember why everybody was Backing Britain; I presume we were in another recession and we were trying to drag ourselves out of it.⁵² That's why the flags were raised. In retrospect, it was a mistake, but there was no way of knowing at the time.

Lockey: I think everybody had been up all night and wasn't thinking very straight.

Sir Christopher Booth:⁵³ During that period I was Chairman of Medicine at the Royal Postgraduate Medical School at Hammersmith, and Hammersmith was, of course, the place that open heart surgery was developed with Melrose's pump based on the Johns Hopkins work.⁵⁴ I think that among the letters published in the *British Medical Journal* at this time, the most interesting was from the Hammersmith group, who were very critical of the whole programme. I have never quite understood why cardiac surgeons at Hammersmith, who had been pioneers in their time, faced with the problems of cardiac transplantation, recoiled in horror and said, 'No.'

Gilston: Just a small point. I think we had all realized that the press is not something to get entangled with. At the first press meeting after the first transplant I was asked how long the tracheal tube would stay in and I said, 'Until it comes out' and that didn't go down too well.

⁵² See the following page for the cover of *Private Eye*, no. 171 (5 July 1968), reprinted with their permission. Five typists at a heating and ventilation firm volunteered to work an extra 30 minutes every day without pay from 1 January 1968 to increase Britain's productivity and initiated the 'I'm Backing Britain' campaign. See Anon. (1968) Backing Britain: The Surbiton revolution. *The Economist* (6 January 1968): 12.

⁵³ Sir Christopher Booth Kt FRCP (b. 1924) trained as a gastroenterologist and was Director of the Clinical Research Centre of the Medical Research Council from 1978 to 1988. He was the first Convenor of the Wellcome Trust's History of Twentieth Century Medicine Group, from 1990 to 1996 and Harveian Librarian at the Royal College of Physicians from 1989 to 1997.

⁵⁴ Dempster W J, Melrose D G, Bentall H H. (1968) Scientific, technical, and ethical considerations in cardiac transplantation. *British Medical Journal* i: 177–178. See also Dr Arthur Hollman's account on page 30 and Melrose's biographical note, op. cit. note 65 below.



Left to right: Professor Donald Longmore, Mr Donald Ross, Sir Keith Ross. Reprinted with permission from *Private Eye*.

Longmore: I was absolutely appalled at the Bentall–Melrose thing [the letter referred to by Sir Christopher Booth above] because they had been working on heart transplantation and had put in a lot of effort and I just could not understand why they, and when we come to the moratorium later, why these people behaved in such an extraordinary way. It was quite amazing.

Now the other thing is the press. I have all the press cuttings here, in order and three bookfuls of them, and they went through the usual routine of the press. Like with Sir Alec Rose,⁵⁵ first of all, ‘What a marvellous man, he sailed round the world alone’, and then, ‘What a disgraceful thing he preferred scraping his boat’s bottom to his wife’, and finally, ‘Why isn’t anybody else sailing alone around the world?’ And we went through this triad of things also. First of all it was, ‘What marvellous chaps.’ Then it was, ‘How awful it is that they did it’, and finally, ‘Why aren’t they all doing it?’ This is a standard press response and I have it all documented here.⁵⁶

Keith Ross: Donald [Ross] mentioned us receiving telegrams. I remember vividly, we got one from Denis Melrose which said, ‘Congratulations, it couldn’t have happened to a nicer bunch of chaps.’

Jane Somerville: There were a number of personal intertwining fallouts of this. One of the things that happened in the Heart Hospital was that everything was kept secret, as a means of trying to deal with the press. When we had our conferences and when we had something about Fred West, the first transplant, we kept it all to ourselves, because that was the order of the day. Now you may remember that Donald [Longmore] had already been disciplined for having even the thought of transplant,⁵⁷ but when it happened in the Heart Hospital there was a very strong body of rather strong people who profoundly disapproved of it. So there we were threading our way between the press – the press and the professors if you like – and the hierarchy of the Heart Hospital, trying to keep this wretched patient alive and to keep everything secret. I was a senior lecturer, which means that I was a junior bod on the professorial unit, and I was threatened with being sacked if I didn’t say what went on in the transplant. I didn’t say, because I thought it was great fun to have a secret anyway, you know. Actually,

⁵⁵ Sir Alec Rose (1908–1991) was a market gardener and fruit merchant from 1945 to 1971, whose recreation was sailing. He circumnavigated the world in 1968, and was honoured with the freedom of the City of Portsmouth in 1968, the City of London in 1969 and became an Honorary Life Governor of the Royal National Lifeboat Institution in 1975.

⁵⁶ Professor Donald Longmore has several folders of national, local and medical press cuttings on heart transplantation from 1966 to 1970.

⁵⁷ See page 8.

subsequently, a couple of months later attempts were made to terminate my appointment.

Bunker: There was considerable disapproval at Stanford as well. Stanford at that time was a very small medical school with a very small hospital, and there is no doubt that Shumway's programmes in cardiac surgery in general and certainly in heart transplant, bumped a lot of other patient care aside, including that of other surgeons who were not pleased to have their cases cancelled for Norm's work.

Joseph: I think it is fair to say that in many ways cardiac surgery was still in its infancy. Apart from congenital work it was mainly valve work up to that time; what Jane says about the disapproval of cardiac transplantation was really an extension of what I saw at the time as being disapproval of cardiac surgery in general. I remember one time vividly when Donald Ross was away and Magdi Yacoub⁵⁸ was the Senior Registrar. Magdi used to go prowling around the medical wards, looking for patients to operate on. It seems strange now, but I think there were an awful lot of patients who merited cardiac surgery, that the cardiologists of the era were not actually referring. Those patients, I recall, became known as 'Magdi's midnight Starrs'.⁵⁹

Treasure: To put that in context, one should know that coronary surgery did not exist at the time. The very first vein grafts were 1967 or so, the first in this country were, I suppose, 1969. But that hadn't arrived, so it didn't exist. But in the same volume of the *British Medical Journal* there's a very interesting article by Richard Emanuel, describing four cases of valve replacement encouraging people, saying, 'Look these people are dying of heart failure with valve disease, and we can fix them, my colleagues Donald Ross and Magdi [Yacoub] could fix them',⁶⁰ so at the time heart surgery at all was a pretty big adventure.

⁵⁸ Professor Sir Magdi Yacoub Kt FRCS FRS (b. 1935) has been British Heart Foundation Professor of Cardiothoracic Surgery at the National Heart and Lung Institute at Royal Brompton National Heart and Lung Hospitals since 1986 and Consultant Cardiothoracic Surgeon at Harefield Hospital since 1969. He was rotating Senior Surgical Registrar, National Heart and Chest Hospitals from 1964 to 1968.

⁵⁹ Dr Joseph wrote: 'After Starr valves.' Letter to Mrs Lois Reynolds, 21 March 1999. Examples of 12 single leaflet disc valves, including the Starr-Edwards Model 6520 manufactured between 1970 and 1976, are on www.csmc.edu/cvs/md/valve/

⁶⁰ Emanuel R. (1968) Too ill for cardiac surgery? *British Medical Journal* ii: 400–402. This article is a tribute to Ross and Yacoub, and describes four patients out of 461 valve replacement operations in the 22 months from 17 December 1965 to 5 October 1967.

Joseph: I must say, I think Jane played an enormous part in what one might call popularizing cardiac surgery amongst cardiologists.

Jane Somerville: I am a failed surgeon, because that's what I really would have liked to have been, not a thinking physician [Laughter]. But I would just like to go back, there's a very interesting thing with regard to the opposition of the hierarchical physicians. They weren't all against it, but Alan Gilston mentioned what we referred to as the 'Night of the Pigs'. They weren't quite transplanted, they were put in series to deal with the stone heart. Unfortunately the pigs got out of the bag that Donald Longmore had, I think, and were squealing as they were trying to be caught and woke up the Matron, who was an absolutely terrible woman, God bless her soul – awful, but hand-in-glove with the Senior Physician about everything. The operation was not a successful one that night and after the hearts had been used, I think it was Donald [Longmore] who sent her the pork chops for her breakfast. Well, that really poisoned both of them. Not only had she been woken up in the Mews with the squeals, but then she had this little plate in the morning, so everybody was reported and I think the antics of the cardiac surgical team and those who supported them, quickly followed by real transplantation, did not endear any of us to the two of them.

Lessof: I was going to say that I am sorry that Richard Batchelor isn't here, because this part of the story, or at least the partial failure of the transplant is the story of the immunology side.⁶¹ Of course the drugs weren't very good, but it wasn't the drug failure really, it was the failure of the tests for rejection. We tried all kinds of things and went by them, because they were the best we had. But people have spoken of their moment of horror. My moment of horror at the Guy's case was at the *post mortem* where the lungs had cannonballs of *Aspergillus* in them, which I had never seen before or since and were clearly related to our drug therapy. The surgical side appeared to be absolutely perfect.

Longmore: Although we are not allowed to be lighthearted here, I just report that the two pigs were delivered into the two mews at the back of the hospital and I was examining one to see if it was suitable and Thompson, the head porter, came in and said, 'Mr Longmore, is that pig in a Land-Rover in the other Mews anything to do with you?' and I said, 'Yes it is.' He said, 'Well it has just got out and turned left along New Cavendish Street' and so in theatre cap, mask and

⁶¹ Professor J Richard Batchelor FRCPATH FRCP (b. 1931) was Professor of Immunology at the Royal Postgraduate Medical School, Hammersmith Hospital, from 1979 to 1994; now Emeritus. See Batchelor R, Clark T, Lessof M H. (1970) Lung transplantation. *British Medical Journal* iv: 306.

boots, I set off after it, and caught it about half-way up Wimpole Street and was driving it back holding its wiggly tail and kicking it and it was 17.00, as Alan Gilston and Eunice will remember, and everybody pretended it wasn't happening, except one fellow who raised his bowler hat and said, 'Excuse me sir, you are going the wrong way along a one-way street.' I had thought this was screamingly funny until the James Bulger case, when that poor child was being dragged round a city by two little thugs being systematically murdered and everybody crossed the street and pretended it wasn't happening.⁶² It's a sad characteristic that people don't actually take any notice of bizarre things.

Dr Arthur Hollman:⁶³ I was a bit surprised at the comments that cardiac surgery wasn't popular in 1968 when I remember that Russell Brock⁶⁴ did the first mitral valvotomy at Guy's in 1948. I was on the Hammersmith team in 1957 and Mr Cleland did the first operation for hypertrophic cardiomyopathy in 1960, a year after we had been to Moscow to demonstrate the Melrose heart–lung machine.⁶⁵ Then I remember that wonderful series of patients done at the Middlesex by Sir Thomas Holmes Sellors⁶⁶ with the support of the cardiologists, Evan Bedford and Walter Somerville, around 1960, and I think over 100 consecutive patients without a single death. I don't understand people's comments that there was a

⁶² James Bulger, aged 2, was abducted from a shopping precinct and murdered on an isolated railway line in Walton, Liverpool, on 12 February 1993 by two ten year olds, Robert Thompson and Jon Venables. See Morrison B. (1997) *As If*. London: Granta.

⁶³ Dr Arthur Hollman FRCP (b. 1923) was a cardiologist at Hammersmith Hospital, London, when the first open heart operations were done in 1957. Subsequently he was on the staff of Great Ormond Street Hospital for Children, London, and University College Hospital, London. Dr Hollman is the official archivist of the British Cardiac Society.

⁶⁴ Mr Russell Claude Brock (Lord Brock of Wimbledon from 1965) (1903–1980) was thoracic surgeon at both Guy's and the Brompton Hospitals from 1936 to 1968. He performed valvotomy for pulmonary stenosis in 1948 and the first mitral commissurotomies in the same year. He edited *Guy's Hospital Reports* from 1939 to 1960. See Brock R. (1981) Personal memories of the early days of cardiac valve surgery. In Snellen H A, Dunning A J, Arntzenius A C. (eds) (1981) *History and Perspectives of Cardiology: Catheterization, angiography, surgery and concepts of circular control*. The Hague: Leiden University Press, 165–172.

⁶⁵ Dr Denis Melrose was assistant lecturer in the Department of Surgery at the Postgraduate Medical School, London, and Surgical Registrar at the Hammersmith Hospital, London, at the time. Melrose D G. (1953) Mechanical heart–lung for use in man (with foreword by Ian Aird). *British Medical Journal* **ii**: 57–62. For details of its application see also Melrose D G, Bassett J W, Beaconsfield P, Graber I G, Shackman R. (1953) Experimental physiology of a heart–lung machine in parallel with normal circulation. *ibid.* 62–66. See biographical note on W P Cleland, *op. cit.* note 85 below. See Cleland W P, Bentall H H, Melrose D G, Goodwin J F, Oakley C M, Hollman A. (1968) A decade of open heart surgery. *Lancet* **i**: 191–198.

⁶⁶ Sir Keith Ross wrote: 'I was Uncle Tom's Registrar in 1957 and Senior Registrar from 1961 to 1967 and his open heart surgery using 30°C hypothermia was universally respected and admired *at that time* and since.' Letter to Mrs Lois Reynolds, 22 March 1999. See biographical note, *op. cit.* note 10 above. See also Sellors T H. (1968) Transplantation of organs. *Veterinary Record* **83**: 530–537.

feeling against cardiac surgery in 1968. Maybe, if I dare say it as an ex-Hammersmith cardiologist, there were one or two at the National Heart Hospital who were against it. It certainly wasn't the case elsewhere in the United Kingdom, for example, Mr Geoffrey Wooler's very good mitral valve repairs in Leeds.⁶⁷

Jane Somerville: I would just like to say that nobody said they were anticardiac surgery, Arthur. They were taken aback. We came from a rather hierarchical hospital, with a Senior Physician from St Bartholomew's who hadn't changed in years, and was Chairman of everything, didn't like women, didn't want them let in the doors. So you can see where we were in the late 1960s, it was a hierarchical hospital, with a powerful group of physicians, and they were a bit taken aback by the rumbustious enthusiasm of cardiac surgeons that, despite their pomposities, life went on and things happened; I think they were not against it, they were just appalled at general manners and what went on. First of all, many of them had no imagination, so that was very difficult to be confronted by this particular group of cardiac surgeons. They were perfectly all right when Uncle Tom was there, 'Yes indeed', and doing everything very politely, but when this gang arrived things got a little different.

Treasure: Well, I think Arthur's point is well taken, we must keep it in perspective, but there are several people here who were housemen, registrars, and the like in 1968, 1969 and 1970, and it wasn't exactly a cake walk doing cardiac surgery at the time, I think that was the spirit of it.

Joseph: I noticed a difference between 1968 or 1969 when I left, and when I came back as a Registrar in 1971, I think, when coronary surgery had got off the ground. There was an enormous difference in attitude in those few years. I think there was certainly a bunch of senior cardiologists in the late 1960s, who just didn't refer cases that should have been referred.

Treasure: I think if anybody wants to cast their minds back, look out the 1968 copy of the *British Medical Journal*, because it's an attempt to remind the public of where heart surgery stood at the time. Richard Emanuel felt the need to write that paper about four valve operations.⁶⁸ So that it wasn't obviously in the mind of every GP.

⁶⁷ Somerville W. (1969) Problems in cardiac transplantation from the cardiologist's viewpoint. *Progress in Cardiovascular Diseases* 12: 174–189. Donnelly R J, Smith D R, Ionescu M I, Wooler G H. (1972) Mitral valve repair: Results at 5 and 10 years. *British Heart Journal* 34: 207.

⁶⁸ op. cit. note 60 above.

Longmore: If I may say, there were two points. First of all the Middlesex. I was Uncle Tom's Registrar or Research Fellow or something when we did the hundred cases without a death, and although Walter Somerville and one or two physicians were very supportive, the general atmosphere was that we were a bunch of renegades. Secondly, and worse, I showed a film, which I still have, of an experimental dog heart transplant in 1964 or 1965 and while I was showing it to the Chairman of the Medical Committee mentioned by Jane, Jane leant across to his colleague and in a loud stage whisper said, 'The man's a liar, it isn't true', and yet there is the film of the thing going in, and that was one of our better dogs which staggered round and bit Charlie, the technician, before it eventually died.

Keith Ross: Just one quick comment if I may, going back to the post-operative phase? As a surgeon and junior member of the team in many ways, the thing that really I found completely foreign to any experience I had had in surgery up until that point was really making no effective contribution in the post-operative management. I still remember the feeling of helplessness combined with the really extraordinary ordeal of these long drawn-out conferences on a daily, sometimes twice-daily basis, when we were all groping with what to do best for this patient, particularly in regard to immunosuppression, in spite of having the help of Dr James Mowbray.

Treasure: Where I would like to take you now just briefly before tea, is a little look at the issues of brain death at the time and how it would be defined. And after tea we will go on to the 'moratorium'. But can I read you something which is from the 1 June 1968 in the *British Medical Journal*, so really very soon after this operation on 3 May:

Inquest on Heart Donor

A verdict of accidental death was returned by the jury on an inquest (*The Times*, 8 May) into the death of Mr Patrick Ryan, whose heart was used in the first British heart transplant operation (*BMJ* 11 May, p. 315). He had been fatally injured in a fall at a building site. Professor R D Teare told the court that Mr Ryan died from lacerations of the brain due to skull fractures, and that he could not have been kept alive even artificially for more than a short time. The Coroner, Mr Gavin Thurston, said that he was satisfied that the transplant team had taken suitable precautions. It was extremely difficult to decide when a man was dead, and this was best left to doctors. Dr E Raftery said that when it had become clear that Mr Ryan's heart could be kept going only by the use of a respirator a decision was made not to attempt further resuscitation, and this was before the transplant team knew of his existence. In his opinion, Mr Ryan had died before he reached the National Heart Hospital. Mr D Longmore, of the

National Heart Hospital, was asked by the Coroner to define death and replied ‘I believe it is not right to accept one single criterion of death....Any definition of death would be dangerous, because if we had defined death five years ago there are many people who are walking around today who would be defined as dead.’⁶⁹

So it was quite interesting. You were obviously drawn out to make that statement. That clearly was a very important issue and, as Professor Bunker has indicated, there was the question of whether he would be indicted for murder in California. Donald Longmore, your recollection of that issue of defining death?

Longmore: Well, there were dozens, hundreds, of press. The coroner’s court was absolutely crammed with journalists and the word ‘murder’ was being circulated around. Mr Gavin Thurston [the Coroner] was faced with a very difficult task, because he had an apparent murderer on his hands. It seemed to me the only thing to do was to fish out of my briefcase the top of the skull which I had taken off and all the photographs of this patient with really the top half of his brain missing – poor Patrick Ryan. That really turned the scales and then we got on to the semantics of the definition of death and I felt very strongly at that time, because there were physicians trying to define death all over the world and had we accepted their definition, what were we going to do with the patients Donald Ross, Alan Gilston and Eunice Lockey and others had resuscitated? Did we then have to shoot them because they were defined as dead and their estates presumably had to be divided? It seemed to me that it was extremely dangerous to have a physician’s definition of death at that time.⁷⁰

Bunker: We had also struggled with the determination of ‘death’ in January 1968 in California. It was still defined in terms of the heart and respiration. The plan at Stanford at that time as elsewhere in the early transplant days was to diagnose irreversible brain damage, withdraw support of respiration, wait for the heart to stop, remove the heart quickly, transplant it to the recipient and then resuscitate it. In attempting to follow this plan we were faced with a semantic quibble, a contradiction in terms. If the heart can be revived, then by definition it was not

⁶⁹ op. cit. note 20 above.

⁷⁰ The Human Tissue Act 1961 made it easier to use organs from dead bodies, by removing the time limit on its subsequent movement and use. Section 1(4) required that the person removing a part be a qualified medical practitioner and be satisfied that life is extinct, although no distinction was made between being ‘legally dead’ and ‘medically dead’. Removal of organs required consent, given by the deceased before death, or by those in possession of the body, effectively the relatives at home, or the coroner, if in hospital (with the relatives’ consent). See Legal Correspondent. (1968) *Medico-Legal: Legal concepts and death. British Medical Journal* i: 389–391. Jennet B. (1980) Brain death. *Lancet* ii: 1306.

dead in the first place. So it was very obvious to us that if you let the heart stop and resuscitate it, it really wasn't dead in the first place, but you certainly jeopardized the success of the operation, so we never did do that.⁷¹

Treasure: Donald Ross – you have been very quiet. What's your recollection of all that and your response to it?

Donald Ross: Well I know that it is a continuing argument still and some of the Muslim countries, I believe, can't accept our brain death criteria and I think it will go on being a controversy for some time. For instance, in Japan they indicted surgeon Jurō Wada for murder and I think Åke Senning in Zürich was also threatened with being indicted for murder if he did a transplant. I don't know if he ever did one.⁷² I think we are not in the clear yet, because there's still an argument about how do you deal with the beating heart donor – it's still repugnant to some people to think that you are taking a beating heart and transplanting it. For them, a beating heart is life.

Treasure: And indeed it is difficult. The multiple donor operation is tough, there is no way of getting away from it and those involved in it have to have a steady nerve and believe they are doing the right thing today.

I now want to start with the issue of the moratorium and talk about that. I would like to refer to some data, which Dr Peter Fleming has very kindly provided for me: in 1968 there were 99 heart transplants. In 1969, 48, in 1970 down to 17, 1971, 9. So after this flurry of activity in 1968 there was a very sharp decline and, as you can see from that list of operations, those who know heart surgeons will recognize all the great surgeons of the era, [Christian] Cabrol and Jurō Wada and so on, whom we have referred to, all did a few, but then it died away and it has been referred to as a clinical moratorium, although we can debate whether that's a useful expression or not.

⁷¹ op. cit. note 45 above.

⁷² Jurō Wada was chief surgeon at Sapporo Medical College, Sapporo, Japan, and performed the world's 32nd heart transplant on 8 August 1968. He was not prosecuted due to lack of evidence. The first Japanese heart transplant following Wada was done on 2 March 1999 under the 1997 transplantation law, which permits the use of organs from brain-dead patients to be transplanted into recipients aged over six. Donors must be over 15 and give written consent, as must the donor's family. See Saegusa A. (1999) Japan's transplant law "is too stringent". *Nature* 398: 95. Åke Senning (b. 1915) was chief surgeon at the Karolinska Institute in Stockholm from 1957 to 1961 when he was appointed Professor of Surgery and Chief Surgeon at the Clinic for Cardiovascular Surgery at the University Hospital, Zürich, Switzerland. Amongst other achievements, he implanted a fixed-rate pacemaker in 1958 – in 1983 the patient was still living, with his 23rd pacemaker. See Senning Å. (1983) Cardiac pacing in retrospect. *American Journal of Surgery* 145: 733–739.

The first thing I want to do is read to you a letter from Sir George Godber,⁷³ who regrets he cannot come, but he was the CMO [Chief Medical Officer] at the time and what he has written to us is:

It is very important that you get this episode right. I fear I cannot now recall the names of the individuals involved, but you will have them. The distinguished surgeon from Guy's who undertook the first two transplants was concerned at the time [and of course that's Donald Ross] about the justification of proceeding with such experimental work. In consultation we agreed to call together the small number of surgeons, cardiologists and clinical physiologists then working in this field to consider whether it would be best to continue work in human patients or to await the outcome of further work in animals. We agreed unanimously on a letter of advice offered by the whole group, which I was to send to the small number of hospital medical staffs working in this field. It was, of course, informal and not simply the CMO's view nor the Department's. It was well received and by consensus, further human transplants were delayed until more research had been done. Of course, someone leaked the letter but it was accepted as a reasonable conclusion by informed people – in no sense an instruction....It is very important that this should be seen as the development of consensus and not central dictation.⁷⁴

That's what he writes as his recollections now, to guide us, if you like, in our discussion of these issues.

There are three people I would like to call on specifically at this point and then other people can join in. First of all, I would like to ask Dr Geoffrey Rivett, who worked in the Department for 20 years, who believes he can help us see the view from the Department of how these sorts of things are handled.

Dr Geoffrey Rivett:⁷⁵ Thank you. George [Godber] appointed me, George has been incredibly helpful to me right up to the last few weeks with writing, and that is a typical [Godber] letter. I would like to put this issue into the wider

⁷³ Sir George Godber GCB KCB CB FRCP (b. 1908) joined the Ministry of Health in 1939, took part in its 1944 survey of hospitals and was active in the introduction of the NHS. He was appointed Deputy to Sir John Charles, the Chief Medical Officer, and succeeded him in 1960, serving the new super ministries of the DHSS, DES and the Home Office, until his retirement in 1973.

⁷⁴ Letter from Sir George Godber to Dr Tilli Tansey, 21 March 1997. For the text of the Department of Health letter, see Anon. (1973) Medical News: Cardiac transplantation. *British Medical Journal* i: 431.

⁷⁵ Dr Geoffrey Rivett (b. 1932) worked in the Department of Health for 20 years, particularly on London issues. He is also a medical historian, whose work includes: (1986) *The Development of the London Hospital System, 1823–1982*. London: King's Fund. (1998) *From Cradle to Grave: Fifty years of the NHS*. London: King's Fund.

context of ‘How does a government department get advice on professional matters if it feels the need?’ Enoch Powell said, in his address to the Winchester branch of the BMA in 1961:

The Minister was not responsible for the prevention, diagnosis and treatment of illness, only for the establishment of a service to secure those desirable ends. At first sight there is a clear division between the Minister who provided the framework and the doctor who followed his profession within that framework. But there was a fuzzy border. In the treatment of a single patient, it was easy enough to keep the Minister at arms length, but if the question concerned the treatment of many patients, the Minister might not know the answers, but he had to find out. The politician was concerned with the general consequences of individual decisions. He resolved the dilemma by creating a professional advisory system. Respectable, august, safe, and therefore in the nature of things, rather elderly. Then, if for example, the General Medical Council declined to approve the qualifications of doctors trained on astrological principles, the Minister could very politely decline to employ them in the Health Service.⁷⁶

Now I don’t know precisely what happened, but the establishment of an advisory group seems to fit neatly into standard Department of Health practice, when there is an issue that is hot to handle and involves matters that go wider than clinical medicine, into finance, priorities, outcomes and ethics.

Treasure: Thank you very much. Now I would like to invite Sir Terence English as a witness, and Dr Renée Fox as an observer of the worldwide scene on this issue of the moratorium. Sir Terence’s name will be well-known to many of you, it was he who started the transplant programme at Papworth, which was the beginning of the new wave, and Renée Fox will address these issues of the clinical moratorium.

Sir Terence English:⁷⁷ The letter from George Godber which you read, effectively established the moratorium on heart transplantation in Britain and was written in

⁷⁶ Powell E. (1961) The elephant and the whale: The Winchester address. *British Medical Journal* i: 1479–1483, quote on page 1480. Powell was then Minister of Health.

⁷⁷ Sir Terence English KBE FRCS FRCP (b. 1932) has been Master of St Catharine’s College, Cambridge since 1993. He was Senior Registrar at the Brompton Hospital, London Chest and the National Heart Hospital, London, from 1968 to 1972 and Consultant Cardiothoracic Surgeon at the Papworth and Addenbrooke’s Hospitals, Cambridge, from 1972 to 1995. He started the first successful heart transplant programme in the UK in January 1979. He has been President of the International Society of Heart Transplantation from 1984 to 1985; President of the Royal College of Surgeons from 1989 to 1992, and President of the British Medical Association from 1995 to 1996.

February 1973. That was three months after I was appointed a consultant to Papworth and two months before I made my first visit to Stanford, where I went to visit Philip Caves,⁷⁸ who had been a registrar with me at the Brompton. I didn't go because of an interest in cardiac transplantation, but while I was there I stayed with Philip for a week and it was clear that he had spent the previous year doing some wonderful experiments in the lab, establishing the use of transvenous myocardial biopsy, which was probably the biggest quantum leap in the management of cardiac transplant patients, because it allowed rejection to be detected that much earlier than previously when you were just relying on summated ECG voltages.⁷⁹ He had been intimately involved with the whole programme and some of that enthusiasm washed off on me and indeed we talked at the time about the possibility of starting cardiac transplantation in Britain. He was determined to do so and I pointed out that there was a good kidney and liver transplant team in Cambridge under Roy Calne.⁸⁰ So when I got back to Cambridge, I contacted Roy and by the end of that year, in October 1973, we had a formal meeting with my surgical colleague, Bill Milstein, the two cardiologists from Papworth, Hugh Fleming and David Evans⁸¹, and Roy Calne, and we discussed the possibility of establishing cardiac transplantation in Cambridge. David Evans made it clear at that first meeting that he was opposed and wished to have nothing further to do with it. We then had various discussions amongst the key surgeons at Addenbrooke's, because of course that's where Roy's base was, and we put a proposal to the Medical Advisory Committee at Addenbrooke's to establish a short programme of open heart surgery. Now everyone knew, or suspected, what this was going to lead to, because Roy had a very busy liver transplant programme going on at the time and there was a lot of opposition to allowing cardiac surgery to be established at Addenbrooke's. Anyway, at the beginning of 1975, we did a series of open heart cases over a period of three months and established the facility in the hospital.

⁷⁸ Mr Philip Kennedy Caves (b. 1941) was Research Fellow and then Clinical Resident at Stanford University from 1971 to 1973 and, along with Margaret Billingham, 'introduced probably the most important single diagnostic tool for the monitoring of cardiac rejection, the endomyocardial biopsy.' Dong E, Shumway N E, Lower R R. (1991) A heart transplantation narrative: The earliest years. op. cit. note 6 above, 435–449, quote on page 444.

⁷⁹ See Caves P K, Stinson E B, Billingham M, Shumway N E. (1973) Percutaneous transvenous biopsy in human heart recipients. *Annals of Thoracic Surgery* 16: 325–326.

⁸⁰ Professor Sir Roy Calne Kt FRCS FRS (b. 1930) was Professor of Surgery in the University of Cambridge and Consulting Surgeon at Addenbrooke's Hospital, Cambridge, from 1965 to 1998. At this time Calne was spearheading the renal transplantation programme at Addenbrooke's Hospital. See Calne R Y. (1979) Immunosuppression for organ grafting – observations on cyclosporin A. *Immunological Reviews* 46: 113–124.

⁸¹ Dr David W Evans was Consultant Cardiologist, Cambridgeshire Area Health Authority (Teaching), at Papworth Hospital and Associate Lecturer at the University of Cambridge.

At the same time, I joined Roy's research programme at Douglas House [an annexe to Addenbrooke's Hospital] where he had for several years been doing heart transplants in pigs, but we were able to bring the anaesthetic and perfusion skills of Don Bethune⁸² and the survival of the pig transplants improved quite substantially. So we had a joint research programme going fairly early. The next thing that happened was in March 1976. We were carrying the debate forward within the hospital at Addenbrooke's when a patient under Professor Ivor Mills presented with a severe cardiomyopathy. I was asked to see this patient, which I did, and he was a man of 59 who was severely cachectic. He had been in hospital for four months and had gangrene of his toes, and I said that I didn't think that he was transplantable. I wrote to Professor Calne that I had seen the patient and then went off to Japan for two weeks on a medical visit. When I got back, I found that all hell had been let loose within Addenbrooke's because Roy had seen the patient (Professor Mills had spoken to him again about it), and he had got Dr Fleming to see the patient, who concurred with my view on things. However Roy still wished to go ahead and I believe was only stopped by the anaesthetists refusing to anesthetize the patient. The patient actually died the day before I got back from Japan. Now I mention this, because it had an important impact on several developments that followed. One was that it totally antagonized Dr Fleming, our remaining cardiologist who was at least prepared to be involved with the programme, and that meant therefore that we had no cardiological support until the arrival of Dr Michael Petch in 1977, who did agree to assist us at the beginning. But it also made things difficult within Addenbrooke's Hospital, and certainly the view amongst the staff there was very much against adding a cardiac transplant programme to the existing liver and kidney one. So I decided the only way we could take things forward would be to do the work at Papworth. This obviously was a disappointment to Roy Calne, who wanted very much to have it under his unit at Addenbrooke's, which is where we'd initially intended it to be.

Now a little later in October 1976, the criteria for the diagnosis of brain-stem death were published.⁸³ This was hugely important, because it meant that I could feel confident about taking a heart out of a brain-dead donor, if that diagnosis had been established by two responsible physicians. So that was a great advance. At the same time, we got funding from the region to do our own research programme at Huntingdon Research Centre, a private institution, and in 1977–1978, we did a series of transplant operations in pigs. These were preservation

⁸² Dr D W Bethune (b. 1934) was an anaesthetist in the Thoracic Surgical Unit at Papworth Hospital from 1970 to 1998.

⁸³ See Jennett B, Hesse C. (1981) Brain death in Britain as reflected in renal donors. *British Medical Journal* 283: 359–362.

experiments, and the most successful of these was one that was sacrificed three months after transplantation, having been immunosuppressed with some cyclosporin which Roy [Calne] gave me at the time, the donor-heart of which had been out of the body for 16 hours. It was a very tough experiment, taking the heart out of a pig on a Monday night and then storing it in the solution that we used, and transplanting it into another pig the next morning. This pig had survived after we had immunosuppressed it, and when we examined the heart after three months it appeared normal. So we then had the basis of experimental proof that if we were to go long distances to bring hearts back to Papworth to transplant, this would be feasible if the quality of the heart was satisfactory to start with. The year 1977 was also important, because the Transplant Advisory Panel (TAP), which had been established by George Godber at the same time as the moratorium, reconsidered the question of heart transplantation.⁸⁴ They took a slightly softer view about the possibility of this happening, and defined the criteria at that time to be met by any group that was considering transplantation of the heart. These criteria were that the centre should be an advanced unit for cardiac surgery with preferably renal transplantation; that donor hearts should be available; that it was important that all the support personnel for transplantation were present and trained, and that this did not impinge on the regular programme of the unit. There should also be adequate support in pathology, immunology and microbiology. Because Professor Calne was on the Transplant Advisory Panel, we became aware of this, and during 1977 I submitted a proposal to the Transplant Advisory Panel, which only met once a year. I therefore had to wait a year until January 1978 before it could be considered, but during that time I wrote to Bill Cleland⁸⁵ and John Goodwin,⁸⁶ who at the time were respectively

⁸⁴ The Department of Health and Social Security's Transplant UK Advisory Panel advised the Chief Medical Officer in February 1977 on criteria to be met by any centre before a cardiac transplant programme could be approved. It also set up a working party to consider criteria for brain death in 1976. The criteria were later considered by two separate subcommittees of the Royal College of Physicians of London and of the Faculty of Anaesthetists, whose report was published by the Conference of Medical Royal Colleges and their Faculties by its secretary, Professor Gordon Robson. A second DHSS committee under Lord Smith drew up a Code of Practice which was, along with the two Conference statements, published by HMSO and delivered to all hospital doctors in January 1980. The two expert working parties were not reappointed after July 1981. See Anon. (1980) Medical News: Heart transplants. *British Medical Journal* i: 654. Pond D. (1980) Brain death. *Lancet* ii: 1306. Robson J G. (1981) Brain death. *British Medical Journal* ii: 505. Health Departments of Great Britain and Northern Ireland. (1979) *The Removal of Cadaveric Organs for Transplantation: A code of practice*. London: HMSO.

⁸⁵ Dr William Paton Cleland FRCP FRCS (1912–2005) was Consulting Surgeon at the National Heart Hospital (from 1994 the Royal Brompton Hospital NHS Trust) from 1948 to 1974; Consulting Thoracic Surgeon at King's College Hospital, London, from 1974 and advised the Department of Health and Society Security on thoracic surgery. [updated 19/1/06]

⁸⁶ Professor John F Goodwin FRCP (b. 1918) was Professor of Clinical Cardiology at the Royal Postgraduate Medical School, London, from 1963 to 1984, now Emeritus. He was appointed

presidents of the Cardiac Society and the Society for Cardiothoracic Surgery. We also accepted two recipients towards the end of 1977, and then met and had some lengthy discussions with the Officers of the Cambridge Area Health Authority. We told them what we were doing and what we wanted to do, and they had a copy of our submission for the Transplant Advisory Panel. That was considered by the TAP in January 1978 and it was very disappointing, because the view taken was that the Department of Health would not favour any one-off operations and that there was no funding to support a proper programme of evaluation. So we were somewhat stymied. However, the Chairwoman of the Cambridge Area Health Authority, Pauline Burnet,⁸⁷ who I must say I had great admiration for, was prepared with her officers to take responsibility for us to use our resources at Papworth for two cases, but it was made clear that that was all the support we could expect. And so this was what we planned to do.

The whole protocol had been based very much on the Stanford programme, with which I was then familiar. I wrote to Dr Shumway in March of 1978 and asked him for some rabbit antithymocyte globulin (ATG), which he was not able to provide.⁸⁸ But we got some equine ATG instead from Upjohn and so we felt we were reasonably prepared. The difficulty then was, we had the money, we had the recipients, but how on earth were we going to get a donor? I wrote to all the neurosurgeons that I knew, and to several anaesthetists, to some of the renal transplanters, asking for help with securing a donor. But, alas, none was forthcoming. Until eventually, in January 1979, we did get a local donor. Roy [Calne] was in fact out of town at the time and Paul McMaster, who was his senior lecturer, agreed that we should use the heart and we did. That was on 14 January 1979. I won't go into details about the operation itself, but in essence the patient, Charles McHugh, suffered a degree of brain damage before being placed on cardiopulmonary bypass. This might have been related to the ATG, which caused a bout of hypotension, and although I was informed of this by Don Bethune before I took the donor heart out, he felt that he couldn't be sure that

Consulting Physician at the Hammersmith Hospital, London, in 1949 and Honorary Consulting Cardiologist at St George's Hospital, London, in 1986.

⁸⁷ Pauline Ruth Burnet CBE (1920–1991) was Chairman of the Cambridge Area Health Authority (Teaching) from 1973 to 1982 having been Chairman of the East Anglian Regional Hospital Board from 1968 to 1974.

⁸⁸ Antilymphocyte serum/globulin (ALS/ALG) and antithymocyte globulin (ATG) are polyclonal antisera to human lymphocytes often prepared in individual transplant centres. The immunosuppressive effects of rabbit ALG on rat thoracic duct cells were reported in 1963. In 1967 ALS was evaluated by a Ciba Foundation Study Group and ALG was adopted in clinical treatment in Denver. See Harkis G D, Caves P, Brown D L, English T A. (1984) Anti-heart antibodies in cardiac allograft recipients. *International Archives of Allergy and Applied Immunology* 73: 18–22. See Cosimi A B. (1988) Antilymphocyte globulin and monoclonal antibodies. In Morris P J. (ed.) *Kidney Transplantation: Principles and practice*. Philadelphia, PA: W B Saunders Company, 343–369.

there was any cerebral damage and that the patient might be all right. Well, we went ahead, and there was indeed brain damage and that patient never got fully off the ventilator, although during the last week of his life he had periods off. But he developed aspergillosis, and died on 31 January. That was a tremendous disappointment to us.

The Transplant Advisory Panel met on 7 February, a week after that, and I was asked to go to the Panel and give them a report as to what had happened. The reaction generally was not favourable, but I said at the time that if Charles McHugh died, we would go ahead and do a second case if we could get another heart. The problem with the Department of Health and the Health Authority during 1979 was compounded by the fact that obviously they detected a lack of harmony in the goals of Professor Calne and myself, in that he still wished to see the work going on in Addenbrooke's, and also to have a full and equal share in the surgical and clinical management of the patient. Indeed, he wanted to do alternate operations and I didn't think this was feasible. Professor Butterfield,⁸⁹ whom we had both trained under at Guy's, and who was then Regius Professor of Physic at Cambridge, was given the unenviable task of trying to mediate between us and get some resolution to this problem and we had a whole series of meetings during 1979.

In August 1979 we did the second transplant, which was for Keith Castle,⁹⁰ and this went very smoothly and successfully, and by the end of 1979, before we did the third case, we had come to an agreement whereby Professor Calne would have a role with regard to providing valuable advice with respect to immunosuppression, and that he would also be involved as an assistant in the next five cases after which we would review the situation. The Transplant Advisory Panel met early the next year in 1980 and they were more impressed with the quality of the last two results. Magdi Yacoub did his first case, I think, just after the TAP meeting in 1980, that would have been in February, and this again concentrated the Department's minds wonderfully on exactly how they were going to handle the development of cardiac transplantation in the UK. I had already suggested that if we could be nominated as the official National Centre, they would find it easier to control things by saying that they weren't going to

⁸⁹ Professor Sir John Butterfield (Lord Butterfield of Stechford from 1988) Kt OBE FRCP (1920–2000) was Regius Professor of Physic at the University of Cambridge from 1976 to 1987 and Master of Downing College, Cambridge, from 1978 to 1987. [updated 19/1/06]

⁹⁰ Halfman M A. (1982) Britain's longest living heart transplant patient: Keith Castle. *Focus on AACN* 9: 24. English T A H, Spratt P, Wallwork J, Cory-Pearce R, Wheeldon D. (1984) Selection and procurement of hearts for transplantation. *British Medical Journal* 288: 1889–1891.

fund anybody else. Then Magdi came along and put his case, and obviously there were now two units in the frame.⁹¹

I managed to raise £50 000 during 1979, which took care of about six cases, and the Department gave us £100 000 during 1980, as a sort of gentle backhander, because they still didn't want to give us the formal recognition that we sought. But then 1980 was in many ways a bonanza year, because our funding came good in that the local millionaire, David Robinson, provided us with £300 000, which was to take care of the two years from 1981 to 1982. The British Heart Foundation also gave me a grant in October of 1980 of £300 000 for establishing a Research Unit. This money was critical at the time, because it enabled us to carry on with the clinical work so that the evaluation by Roy [Acheson] and Martin Buxton and their two teams on the cost-effectiveness of the transplant programmes at Harefield and Papworth was able to be completed and the final report was published at the beginning of 1985.⁹² The results were such that both units then got supra-regional funding and our futures were secure and I think that is where I should stop.

Treasure: Thank you very much, Sir Terence. I think you are a master of understatement with some of the comments you made, just as Donald [Ross] made light of his surgery. I think some of those negotiations had tensions which you brushed aside. A lot of people have memories of that which I want to come on to later, but first can we ask Dr Fox to give us some comments, some perspectives of this issue of a clinical moratorium.

Professor Renée Fox:⁹³ Before I speak about the issue of clinical moratoria more generally, let me just say that historically speaking, 1968 – especially the months of September to November 1968 – was the time of a heart transplant 'boom' on a world basis. It was a bandwagon period internationally and the figures I have are that 105 cardiac transplants were performed in that year, 60 of them over the course of September to November alone. After November 1968, the number of human transplants the world over took a sudden sharp plunge and levelled off. Most surgeons, it would seem, did only one heart transplant and then stopped. By 1 December 1970, a total of 167 heart transplants had been recorded. These

⁹¹ See biographical note, *op. cit.* note 58 above. The units were approved for supra-regional funding by the Department of Health and Social Security in 1986.

⁹² *op. cit.* note 14 above. Use of Cyclosporin A began at Papworth in March 1982.

⁹³ Professor Renée Fox (b. 1928) was Annenberg Professor of the Social Sciences at the University of Pennsylvania from 1969 to 1998, now Emeritus, with secondary joint appointments in the Department of Psychiatry, Department of Medicine and the School of Nursing. She was George Eastman Visiting Professor at Balliol College, Oxford, during 1996–1997. See Fox R C, Swazey J P. (1992) *Spare Parts: Organ replacement in American society*. New York, NY: Oxford University Press.

are the National Institutes of Health figures⁹⁴ in the United States. But then over the period between December 1967 and the fall of 1970, of the 64 teams that had engaged in heart transplants, two of them, Norman Shumway's and Denton Cooley's,⁹⁵ had done more than 25 per cent of the total and by 1970 only Dr Shumway's team was doing heart transplants regularly, averaging one per month. Dr Cooley had a very high mortality rate. By September 1969, all 23 of the patients on whom he had done cardiac transplants were dead. In contrast, as of October 1970, nine patients survived out of the 27 heart transplants Dr Shumway had performed.

I would say that after these couple of years, this period that I cited from December 1967 to the fall [autumn] of 1970, what could probably be called a clinical moratorium on heart transplants came to exist. The microdynamics of why different teams stopped, may have differed but the overall aggregate effect was to bring heart transplantation largely to a halt, except in the context of Dr Shumway's team, until approximately 1980, when there was a new take-off in cardiac transplants. I associate that, not exclusively, but nevertheless, integrally, with the advent of the immunosuppressive drug, cyclosporin,⁹⁶ which seems to have played a very important, though not singular role in starting the process up again.

This pause and slow-down in cardiac transplantation belong to a larger and recurrent phenomenon in the dynamics of therapeutic innovation that came to be called a clinical moratorium. What's involved here begins with the trajectory from the laboratory phase of medical research and work on animals, its progression to the clinic and to human subjects, and the ambiguity about when the time has come to conduct patient-oriented clinical trials. That's one factor. Moving from the laboratory to the clinic, whenever it occurs, is inherently premature because of the problem of the relationship of the animal to the human model, because of the problems of known and unknown uncertainties, because of the high risks that are involved and the minimum of benefit that is likely to result for patient-subjects at

⁹⁴ See Fox R C, Swazey J P. (1984) *The Courage to Fail: A social view of organ transplants and dialysis*. Chicago: University of Chicago Press. The data referred to above is illustrated on page 128.

⁹⁵ Dr Denton Cooley (b. 1920), was a Consultant in cardiovascular surgery at St Luke's Episcopal Hospital-Texas Children's Hospital and Surgeon-in-Chief of the Texas Heart Institute, as well as Clinical Professor of Surgery at the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, Houston, Texas. He performed his first heart transplant on 2 May 1968, with a further 11 by the end of the year, including one xenograft using a sheep heart and one heart-lung transplantation. Of these 12, seven died. See Cooley D A, Hallman G L, Bloodwell R D, Nora J J, Leachman R D. (1968) Human heart transplantation: Experience with twelve cases. *American Journal of Cardiology* 22: 804-810.

⁹⁶ Cyclosporin A was used on all patients at Stanford from December 1980. See Morris P J. (1981) Cyclosporin: Overview. *Transplantation* 32: 349-354.

that particular historical juncture. Quite typically, as has been described this afternoon, the new therapy at this stage in its development constitutes a desperate remedy for patients who are already desperately ill, which complicates the outcome, makes it difficult to interpret and usually means that the survival time of the patient–subject is short, though there is ambiguity about what should be considered to be a short and a not-so-short survival at this stage. There’s also a considerable amount of iatrogenic harm caused by the new procedure or drug that is likely to result at this time, partly because of all the problems of uncertainty of technique, of dosage, and the like that are involved. The mortality rate at this point in the development of a therapeutic innovation is inevitably very high. In the case of the early history of human organ transplantation, then after the first couple of years of a heart transplant ‘boom’, a clinical moratorium seems to have taken place, which I define as a suspension of the use of a still-experimental procedure on patients, which may last for weeks, months, or years.

Moratoria have occurred repeatedly in the history of therapeutic innovation and also repeatedly in the history of organ transplantation, not only with regard to cardiac transplantation. Typically, a moratorium takes place when the uncertainties and risks of a new treatment became sharply apparent and the patient mortality rate seems unbearable or unjustifiable. Under those circumstances, pressure for a moratorium can come from the physician investigators’ own reactions to the situation, from their colleagues in various ways, through face-to-face interaction, through what they publish in medical journals, from the institution in which they work, or from patients and their families. This is the way I defined a clinical moratorium at the time that I wrote about it,⁹⁷ but I would add to this now that the pressure to cease and desist can also come from the media, as you have dramatically exemplified today, and growingly from ethics committees within hospitals or extramural independent bodies like the Nuffield Foundation’s Council on Bioethics or, increasingly, executive, legislative or judicial political bodies, including royal and presidential commissions and their equivalents. I think these additional sources of pressure are developments that are associated with the emergence of bioethics since the beginning of the 1970s. It has increased organized attempts to regulate patient-oriented clinical research from outside as well as from inside of the medical profession.

The major precipitant of the moratorium in the early history of cardiac transplantation seems to have been the high mortality rate associated with the gravity of the patient–subjects’ illnesses and their terminal stage. In addition, the short-term acute rejection and chronic rejection were coupled with the danger of

⁹⁷ *op. cit.* note 94 above, 122–148.

massive infection under the immunosuppressive regimes that were then available. Furthermore, coronary artery disease developed in certain recipients' new hearts, for example in the case of Dr Philip Blaiberg, the second patient on whom Dr Christiaan Barnard operated, the development of myocardopathy in others and also an immune response to the grafted heart. Surgical technique did not seem to be as contributory a phenomenon, as was the case with early liver transplants. A clinical moratorium was called on liver transplants at a certain point by Thomas Starzl in the United States, and I think by Sir Roy Calne as well, in order to go back to the laboratory to work on the complicated surgical techniques for liver transplantation, that they felt were deficient at that particular time.⁹⁸ The rejection reaction phenomenon was a major problem. No back-up existed in the form of the artificial kidney machine as in renal transplantation. Nobody has mentioned it today, but I found in the literature an original assumption that the heart might be, and this is the phrase that was used, 'a privileged organ' that would not be subject to rejection like other organs are – an assumption that doesn't seem to be scientifically based and that proved false. The moratorium entailed a mixture of responses to different kinds of pressure from physician investigators themselves, colleagues, medical institutions, patients and their families.

In the case of Dr Pierre Grondin⁹⁹ in Montréal, Canada, who called a moratorium on cardiac transplantation, pressure upon him came from his own hospital and also from what the French might call 'a prise de conscience' on his own part. He was very admiring of Dr Denton Cooley and as Dr Cooley's mortality rate got more and more daunting, his role model seemed less and less exemplary to him in that regard. But Dr Cooley himself, as he put it rather inelegantly at the time, stopped doing heart transplants because 'his stream of donors had dried up.' I assume that what was happening is that his colleagues were not referring patients to him any more for cardiac transplants the way they had before, and that perhaps patients, and patients' families, were less enthusiastic about this procedure.

⁹⁸ Dr Thomas Starzl (b. 1926) was Chief of Surgery at the Veterans Administration Hospital, Denver, and Professor of Surgery at the University of Colorado School of Medicine, Denver, from 1964 to 1980, when he moved to the University of Pittsburgh Medical Centre as Director of the Transplantation Institute. See Starzl T E. (1992) *The Puzzle People: Memoirs of a transplant surgeon*. Pittsburgh: University of Pittsburgh Press. Starzl suggests the moratorium on liver replacement was in its third year at the time of the Ciba symposium on ethical problems arising from transplantation. See Wolstenholme G, O'Connor M. (eds) (1966) *Ethics in Medical Progress: With special reference to transplantation*. A Ciba Foundation Blueprint. London: J & A Churchill Ltd.

⁹⁹ Dr Pierre Grondin at the Montréal Heart Institute agreed to a moratorium following pressure from the Director of his Institute, his colleagues and the transplant committee. All nine of his heart recipients died. op. cit. note 94 above, 144.

I might add that the pressures for a moratorium can be internal or external, formal or informal, explicit or implicit, and a mixture of all of these was involved. Just to give you an illustration of what I mean by implicit and not totally formal, there is a wonderful historical example in the development of heart surgery of the 17-year moratorium that was called informally, implicitly and quasipassively throughout the medical and surgical professions the world over. This is the moratorium that Elliot C Cutler called on mitral valve surgery in and through his co-authored article with Claude S Beck.¹⁰⁰ That article reviewed the total of 12 operations that were reported for chronic valvular disease of the heart at that time through 1928, including seven that had been carried out by Dr Cutler himself, three valvulotomies, and four valvulectomies. All died in a matter of hours or days, except for a fingered dilatation for aortic stenosis carried out by Cutler in 1912, and for the first patient on whom Dr Cutler operated for mitral stenosis in 1923, who died four years and six months later. A telling indicator that the mortality rate doesn't go in a nice neat kind of a progression, one of Dr Cutler's earliest patients did far better than any other subsequent patients. Dr Cutler signalled that he was stopping simply through the subtitle of his article which was called 'Final report on all surgical cases.' The message seems to have been tacitly received by the medical and surgical professions throughout the world because so far as I know no-one attempted microvalve surgery after that until November 1945, when Charles Bailey in Philadelphia performed a valvulotomy, which incidentally was a failure, at least the first one that he did.

Let me just end by saying that there have been numerous other moratoria that have occurred in the history of organ transplantation; for example there have been several moratoria on xenotransplantation. Dr Hardy attempted one in 1964 and stopped.¹⁰¹ Dr Keith Reemtsma¹⁰² and Dr Thomas Starzl have made attempts, as you know, with baboon organs¹⁰³ and also Leonard Bailey with the Baby Fae case

¹⁰⁰ Professor Elliott Cutler (1888–1947) was Professor of Surgery at Harvard University. See Cutler E C, Beck C S. (1929) Present status of surgical procedures in chronic valvular disease of heart: Final report on all surgical cases. *Archives of Surgery* **18**: 403–416.

¹⁰¹ A 68-year-old man received the heart of a chimpanzee on 23 January 1964 in University Hospital, University of Mississippi Medical Centre, Jackson, Mississippi. See Hardy J D, Chavey C B. (1968) The first heart transplant in man: Developmental animal investigations with analysis of the 1964 case in the light of current clinical experience. *American Journal of Cardiology* **22**: 772–781.

¹⁰² Dr Keith Reemtsma (b. 1925) was Associate Professor, later Professor of Surgery at the Department of Surgery at Tulane University School of Medicine, New Orleans, from 1963 to 1996 before moving to the University of Utah College of Medicine as Professor and Head of Department of Surgery. Reemtsma's chimpanzee kidney grafts took place in autumn 1963. See Reemtsma K. (1991) Reflections of a xenotransplanter. op. cit. note 6 above, 553–564.

¹⁰³ Starzl's Colorado team gave baboon kidneys to six patients. op. cit. note 98 above, 113.

in 1984 and each of them stopped.¹⁰⁴ Most recently, since I have been in England this year, a moratorium has been called here on xenotransplantation by the former Secretary of Health. There have also been several moratoria on the use of anencephalic donors. Adrian Kantrowitz attempted one very early.¹⁰⁵ More recently Leonard Bailey at Loma Linda did one in July 1988.¹⁰⁶ In each case these were attempted and then they were stopped. I have already mentioned the moratorium on liver transplantation, going back to the laboratory to work on surgical technique. Also there has been a moratorium called on cluster transplants in children, multiple organ abdominal transplants, as a consequence of a mixture of pressures, partly enforced on Dr Thomas Starzl, partly initiated by him. And although this is not quite strictly about organ transplantation, as you know in April of this year a moratorium was called here in this country on the use of the battery-operated pump to take over the action of the heart, which was used in Papworth and also at the John Radcliffe Hospital, called by Dr John Wallwork, Director of Transplantation at Papworth. In fact some of the organ transplantation moratoria connected with cardiac transplantation have a kind of symbiotic relationship in certain ways to the story of the recurrent attempts to implant an artificial heart, either a whole artificial heart or a more modest, bridge-to-transplant ventricular device. I personally had the opportunity to study the rise and the fall of the Jarvik-7 artificial heart in which a quite spectacular moratorium was finally called.¹⁰⁷

¹⁰⁴ Bailey L L, Nehlsen-Cannarella S L, Concepcion W, Jolley W B. (1985) Baboon-to-human cardiac xenotransplantation in a neonate. *Journal of the American Medical Association* 254: 3321–3329. The recipient survived 20 days.

¹⁰⁵ A male anencephalic infant was used as a donor on 6 December 1967 in Maimonides Medical Centre, Brooklyn, New York. See Kantrowitz A, Haller J D, Joos H, Cerruti M M, Carstensen H E. (1968) Transplantation of the heart in an infant and an adult. *American Journal of Cardiology* 22: 782–790.

¹⁰⁶ Goldsmith, M F. (1988) Anencephalic organ donor program suspended – Loma-Linda report expected to detail findings. *Journal of the American Medical Association* 260: 1671–1672.

¹⁰⁷ Dr William DeVries inserted a permanent artificial heart, designed by Robert Jarvik, in a 61-year-old patient on 1 December 1982 at the University of Utah. The patient lived 112 days. Other designs were implanted until the FDA suspended their use in 1990. Professor Renée Fox wrote: ‘Dr William DeVries did not only perform the implant of a Jarvik-7 artificial heart in Barney Clark on December 1-2, 1982, at the University of Utah Medical Centre in Salt Lake City. Subsequently, at the Humana Hospital Audubon in Louisville, Kentucky, he implanted Jarvik-7 artificial hearts in William Schroeder on November 25, 1984 (who survived 620 days); in Murray Haydon, on February 17, 1985 (who survived 488 days); and in Jack Burcham, on April 14, 1985 (who lived only 10 days post-operatively).’ Letter to Mrs Lois Reynolds, 28 March 1999. op. cit. note 93 above, 95–153. For a recent history of attempts to produce an artificial human heart, see the BBC2 *Horizon* programme, ‘Electric Heart’, broadcast on 18 February 1999.

Treasure: There are fascinating ideas there, I think, of the notion of a moratorium. Do you know Dr John Wallwork here or Mr Wallwork as we call him? John, why don't you join in?

Mr John Wallwork:¹⁰⁸ I think you should go back to the true story. There are two slight errors of fact. I didn't call for a moratorium on the artificial heart, I said we closed our proposed pilot study, because we needed to have a larger *n*-number and indeed we have a great interest still in doing artificial hearts and I am about to continue to do that. With regard to xenotransplantations, I think that our interpretation of the Kennedy Report is not a moratorium.¹⁰⁹ The Kennedy Report very carefully set out guidelines for what we need to proceed towards before we do xenotransplantation, which is what we have already decided we wanted to do anyway, which is more research, generally with immunosuppression and obviously a safety board. So I don't think it called for a moratorium, but I think the Kennedy Commission does exemplify the hurdles we have to go through now to introduce new technology into the Health Service compared with what happened in 1968. I wish in many ways that I had done a xenotransplant two years ago, before we got involved in all the committees that we are involved in now, but we decided to go the right route and rather than the traditional bombastic surgical route.

Fox: I don't want to be misunderstood. A moratorium as I am defining it, but perhaps you don't agree with that definition, is not necessarily a ban or an interdict. It can involve the act of going back to the laboratory, rather than continuing for the time being on the clinical level.

Wallwork: I understand, but we haven't done the clinical work yet, so we can't go back. We haven't gone anywhere to go back from.

Fox: I think there is at least one other phenomenon that should be added to an understanding of the dynamics of a clinical moratorium. Xenotransplantation

¹⁰⁸ Mr John Wallwork FRCSE (b. 1946) first became involved in heart and heart-lung transplantation as a Fellow in Cardiovascular Surgery at Stanford University Medical School from 1980 to October 1981, when he was appointed Consultant Cardiothoracic Surgeon at Papworth Hospital, Cambridge. He has been Director of the Transplant Service there since 1989 and Medical Director of Papworth Hospital since April 1997.

¹⁰⁹ Professor Ian M Kennedy (b. 1941) has been Professor of Health Law, Ethics and Public Policy at University College London since 1997. He chaired the Advisory Group on the Ethics of Xenotransplantation from 1995, whose report, *Animal Tissue into Humans*, was delivered in summer 1996 and published in January 1997 (London: HMSO), supposedly delayed by the Department of Health. As a result, the Government placed a moratorium on clinical trials and xenotransplants in order for more research to be done on the danger of passing pig viruses to humans. The UK Xenotransplantation Interim Regulatory Authority (UKXIRA) first met on 17 July 1997, chaired by the former Archbishop of York, Lord Habgood of Calverton, who took a PhD in the Physiological Laboratory in Cambridge in the early 1950s.

and also gene therapy and genetic engineering present this phenomenon, because undertaking these procedures or stopping them once they are initiated involve taking into consideration the harm that could be done to the whole human population and not simply to the particular individuals who might be the subjects of those therapeutic innovations.

Treasure: Can I ask just one question of Donald Ross, because Sir Terence said he was given the funding to do two [transplants] and obviously just ten years later there was a financial constraint, there were purse strings that he had to persuade to be opened. Who funded your two transplants? Was that discussed? What was said about it?

Donald Ross: It wasn't discussed at all. It was just done as a routine case, but I don't like the term moratorium very much. It implies some higher authority, saying 'stop'. Really I was part of that clinical moratorium which was a self-imposed moratorium as far as we were concerned. After our early euphoria we realized that we were abysmally ignorant and didn't know how to assess rejection or how to treat it. Our second case was basically a failure. At that stage I made a decision that I would do one more and that would be it – either it would work or not. We did another one, which didn't work very long, and that triggered my self-imposed moratorium, which I think applied to most of the people working at that time when the great fall-off occurred. So it implies that the surgeons did have a sense of responsibility and then, of course, the Government moratoria came into play. However, I think doctors should be given some credit for a sense of responsibility in this respect.

Treasure: Quite right, Donald, and I think your point is an excellent one and it is within the spirit of what Renée was saying, but was slightly lost sight of. It was the same with Cutler, it was Cutler who said, 'This isn't working, let us stop.' Nobody told him to stop.¹¹⁰

Fox: The 'Final report,' said, basically 'I am not going to do any more mitral valve surgery' and implied, 'I think it might be dubious for anybody else to do it', but it was self-imposed.

Keith Ross: To have a moratorium, or a decline, or whatever terminology you use, you have first of all to have an upward surge. My question is, how much do people here, who know about these things, feel that the explosion of cardiac transplantation in the late 1960s was directly due or partly due to the word that tissue typing was the sort of open sesame to successful organ transplantation?

¹¹⁰ For later discussion of Cutler's decision, see Beck C S. (1954) The technique of opening the stenotic mitral valve. *Journal of the American Medical Association* 156: 1400–1401. op. cit. note 100 above.

Fox: Could I tackle that? One thing, and this may seem less medical than you would like, but the powerful symbolism of heart transplantation which Dr Somerville was involved in, the meaning of the human heart, the audacity of taking the heart out of one person and putting it in another, the tremendous drama that was involved in that, I think contributed a great deal to the transplant boom. As a matter of fact, the image that was invoked earlier this afternoon, of the transplant team waving Union Jacks at a press conference¹¹¹ is not a laughable phenomenon. The fact that all over the world, in various countries, teams felt attracted to doing at least one such transplant, had a very nationalistic dimension to it. Doing a heart transplant in that particular year of the transplant age was tremendously important for reasons that were not purely medical and surgical.

Keith Ross: I wasn't for a moment going to deny that. But my question still stands. I think that there was a certain responsibility for the boom in terms of reliance on tissue typing.

Treasure: Sir Terence, what about that question?

English: I think that most clinicians are optimists and certainly when tissue typing came along there were many renal transplanters who saw it as being the Holy Grail, which was going to make life very much easier, but it didn't turn out that way. But yes, I think it did add a boost. I have been asked by our Chairman to comment on the question of cyclosporin and how this affected the question of kidney transplantation in the early 1980s.¹¹² I think it had a huge impact. It was used first clinically by Roy [Calne] in kidney transplantations in 1978 and then it was used in heart transplantation in 1980 when John Wallwork first had experience of it while he was at Stanford, and it was introduced into our programme in March 1982. And if you look at the rise in interest in cardiac transplantation from the international register, there was a huge increase from 1983 to 1985. Before cyclosporin, acute rejection was very dramatic. All one had was azathioprine, steroids and ATG [antithymocyte globulin]. The patient might be fine one day and dead the next. Cyclosporin attenuated acute rejection and gave one a chance to deal with it. So it did, indeed, have a huge impact. It is, however, a drug with some nasty side-effects.

Jane Somerville: For want of a better term, the clinical moratoria, or the reduction in numbers or the absence, I think was very strongly related to the difficulty in acquiring donors. I think the press, whose habits were upheld by the Press Council, behaved in a disgraceful fashion. I think people were genuinely

¹¹¹ op. cit. note 52 above.

¹¹² op. cit. note 88 above.

fearful of having all these people, only doing their job, but running through their homes, making their moment of bereavement just terrible. There were many complaints at the time, and I think this was a major factor. I respect what Donald [Ross] says, but I think if they'd had donors they would have soon found recipients. That's number one and the second thing is I am very interested in your comments on what Cooley said. I am not at all surprised that he ran out of donors, because he used to say in the late 1960s when the riots were on, 'Shoot for the head, fellows.' I mean there was a banner headline in an American paper, 'Dr Cooley says shoot for the head.'

Dr David Tyrrell:¹¹³ I'd like, if I may, Sir, to take a wider view of this problem. I'd like to call it, 'A pause for thought' in the introduction of new technologies and new medicines, because I have seen it in different contexts. For instance, early in the development of molecular biology, it was found that you could put human genes into *Escherichia coli*. There was great excitement and there was great apprehension, and in fact a moratorium was called. The message came forth from California, 'Stop, because we really need to know what we are doing before we proceed any further.' In some places there was some degree of legal control over it, but by and large it was an example of the scientists saying, 'Let's sit down and think how we can conduct such experiments without endangering people.' We didn't want *E.coli* in our food and perhaps pouring out insulin and doing us great harm. So there were committees meeting everywhere and talking without facts a lot of the time and guessing quite wrongly about how rapidly techniques would improve and that there would be benefits and not just disadvantages. When I was involved with the Nuffield Foundation one of the thoughts of the Trustees was that we seem to leave these things until the discovery is made and then we have a panic. Wouldn't it be better if we tried to anticipate a new advance in biology or medicine and think about the implications, ethical, practical first, so that when the new situation arrived we would not have a sudden stop. We could say we had thought this through and we agreed how to proceed. That was the main reason for the Nuffield Council on Bioethics being set up, though it was partly because the Government didn't want to do it. But I do think it has proved to be a good idea difficult to implement. My thought at the moment is to look back at what's happened in cardiac surgery and perhaps see if one can learn from that how to use this type of mechanism more effectively in future. I think something like this is

¹¹³ Dr David Tyrrell CBE FRS FRCP FRCPath (1925–2005), physician, virologist, previously Director of the MRC Common Cold Unit, Salisbury, from 1982 to 1990 and Deputy Director of the Clinical Research Centre, Harrow. He served as a Trustee of the Nuffield Foundation from 1977 to 1992 and on committees concerned with clinical research ethics, genetic manipulation and use of dangerous pathogens. See Tansey E M, Reynolds L A. (eds) (1998) The MRC Common Cold Unit. In Tansey E M, Christie D C, Reynolds L A. (eds) *Wellcome Witnesses to Twentieth Century Medicine*, vol. 2. London: Wellcome Trust, 209–268. [updated 19/1/06]

going to happen again and again, and we need to find better ways of handling it if we possibly can.

Treasure: Thank you very much. Now I know Renée Fox wants to come back into this and she has given this a great deal of thought and knows a great deal about it, but I want Professor Longmore to tell us what actually happened in this case, because he remembers it well and has studied it also.

Longmore: Well, Chairman, indeed I have been through all the records in the Department of Health of the various committees, and I think Professor Fox has given us a brilliant overview of a different country. We have two pressures here which are unique.

First of all, apart from the nutters who believe that there's a fifth ventricle with God in it and so on, and I have a lot of letters from people particularly who have had sex changes who feel that life isn't worth living, who would like to be heart donors. Coming to the more serious issues, we have a popular press in this country which is nationwide, not local as it is in the United States, and the press has always compared the results of the new with the theoretical ideal rather than comparing them with what actually happens at the moment. And so if something new comes along and it doesn't work absolutely perfectly, then it is heavily criticized until such time as they get bored with that and say, 'Why aren't you doing it?' The much bigger pressure we have is the Department of Health and the Ministers of Health and I really don't want to quarrel with Geoffrey Rivett, but I have been through all the records in the Department of Health and they are in contrast to what I think we all believe. First of all, the first response of the Department of Health was to say, 'My God, this might work, it's going to cost money, how much money?' and they did a lightning survey of the costs of all kinds of medical procedures all over the UK, and what that revealed was that hospitals hadn't the slightest idea how much things cost, that was a 400 per cent difference in the cost of a valve replacement between hospitals A and B, and nobody really knew what anything cost and in particular nobody could estimate what a heart transplant would cost. So what they then did was say we need a heart transplant unit with 24-hour cover, with *n*-number of nurses, *n*-number of pathologists and this is going to cost that much, my goodness it's too much, we can't do it. Now having taken that decision, which is all documented in the Department of Health – the records will all be burnt under the 25-year rule, if we don't get on and filter them out – having taken that decision, the next stage was to set up committees, and one committee has 40 members, of which one had a passing knowledge of heart transplantation and none of the others, and many of the names I know to be implacably opposed to it. These committees never

discussed the moral, ethical, legal considerations, only the cost and how the procedures could be stopped.

We now come on to two people, Terence English and Magdi Yacoub. These two behaved very differently towards the Department of Health and elicited extremely different responses. Terence was meticulous in writing to the Transplant Advisory Committee [Panel], writing to his regional board, everybody you could think of, explaining what he wanted to do, why and in one or two letters even how much it was going to cost, and the conclusion, after all that meticulous effort on his behalf to try to inform everybody, of one of the meetings was: 'Terence English is trying to do heart transplantation by stealth, by getting money from other sources.' So that's one person. Now the other one is Magdi Yacoub, and the Department of Health had a different problem with Magdi, because whereas Terence has written all the letters that he should have done, Magdi never did, and there's a wonderful letter in the files from Ken Clarke, would-be leader of the Tory party to John Patten and it goes like this:

Dear John, This 'mad' surgeon at Harefield is clearly trying to do transplants. How can we stop him? Perhaps the best way would be to close Harefield Hospital and to move it to Northwick Park, but don't forget, for God's sake, not to let them know what we are up to.

Now that letter exists in the files from one Minister to another and there's nothing medical in that at all, it is simply political money. And Terence overcame that by getting his millionaire's support and we are not quite sure how Magdi overcame it, but probably by just pressing on. And so I think it is terribly important for us not to be God-like and think we have had a moratorium, because doctors thought it wasn't right and so on, it was forced on everybody. The thing that really saddens me is the duplicity of many of our colleagues, who were saying, 'Jolly good chaps, you must try, you must go on' and who were at the same time sitting on these committees at the Ministry, and what they've said is minuted and planning how on earth they can stop from Terence from going on, how they can stop Magdi.¹¹⁴

Treasure: What sort of date are you talking about?

¹¹⁴ Harefield Hospital, Uxbridge, London, is likely to close with Professor Yacoub's expert team to be moved to a £200m super-hospital planned for derelict land next to St Mary's Hospital in Paddington Basin. The Royal Brompton Hospital in Chelsea, which merged with Harefield in 1998, would also be closed with some staff transferring to the new heart unit. Waugh P, Laurance J. (1999) Harefield Hospital to be shut. *Independent* (2 January 1999): 7.

Longmore: The records for the 1960s have got burnt, because the Department of Health burn the records after 25 years. Fortunately they are terribly inefficient, and they don't get all of them, and if Dr Tilli Tansey is quick off the mark, I can give her the source of these records.

Treasure: But to get the perspective, of course, the two are not contradictory. It could well be, and I believe it was, that in 1969 the consensus as spelt out by Godber, described by Donald Ross, and Keith Ross and Barry Ross from what they have told me, would have gone along with it, was, 'Hang on, pause for thought.' It was the difficulty in getting it restarted. They are not contradictory.

Longmore: There was an interim period between 'let's just stop and think a bit' and the people trying to get going again, during which time the Department of Health regrouped its committees and, as I say, one committee has 40 people sitting on it and only one has a passing knowledge of heart transplantation and the others are implacably opposed to it. So we must bear in mind that the two people who started it again, started it against tremendous odds. In other countries medicine isn't centrally organized, it isn't efficiently organized in the way we are, and they don't have the gutter press to help them and these are really the two salient points I want to make, just emphasizing the duplicity of some of our colleagues who really should be ashamed of themselves and if the records could be published, I don't know how they would explain themselves away. I think I have said too much.

Rivett: One must accept that many decisions in the NHS are taken against a financial background, and let us not forget that while in the 1960s there was reasonable growth, in the early 1970s we had the oil crisis and recession. At the same time the control of management on clinical matters was tightening. Earlier control had been more gentlemanly.

Longmore: I think Geoffrey Rivett is too nice for this world.

Dr Walter Somerville:¹¹⁵ Can you stand another Somerville? You will have to for a moment. I would like to address my brief comment, let me see how shall I put it? I think it seems from the discussion that those more knowledgeable than I have said that 1980 was an *annus horribilis* for transplantation, about at that time.

¹¹⁵ Dr Walter Somerville FRCP (1913–2005) was Honorary Physician to the Department of Cardiology at the Middlesex Hospital, London, from 1979, having been Physician from 1954, and to the Cardiac Surgical Unit of Harefield Hospital, Uxbridge, Middx, from 1952 until 1978. [updated 19/1/06]

If I can put this remark to Terence. If you can transpose yourself from today to 1980, when you were in the thick of what sounds like an awful dilemma about what should be done and if you were to point out what you would do if you were back in 1980, what step, what single most important step, would you take to shorten the interval between 1980, the 1980s to 1990, and thereafter, when cardiac transplantation appeared to have a new life. It may be immunology, but I don't think so, because practically everything you referred to in immunology was already well known by 1980 and yet why was it not applied, was there any sort of internecine war between cardiologists and immunologists, was there any personal internecine war between competing elements?

English: I will try and answer that question, Walter, but I suspect that I might not answer it very satisfactorily. If I position myself at the beginning of 1980 in the UK, I see a situation in which there have been three transplants done; the first one failed, the second two apparently successful. There had been this gap of nearly ten years between the moratorium and the restarting. Certainly I felt under enormous responsibility to try and get it right this time. Not just the immunology and the general management, but the publicity and some of the other things that we were talking about earlier. And at the same time there was a considerable anxiety amongst the medical profession that it wasn't going to work. Foremost within that group were some cardiologists who really didn't think that it was going to bring anything but further problems and disrepute, and this and its impact on public opinion was the most important issue at that time. The biggest problem for our programme came in September 1980, when Michael Petch¹¹⁶, after very careful thought, decided that he was going to withdraw his cardiological support. Up until that time he had been part of it [as cardiologist]. We had assessed all the patients together and only accepted a recipient if we both agreed that it was the right thing to do, so there was a complete sharing of responsibility for recipients. In September 1980, and I think largely under pressure from his two colleagues, he decided that he wanted to pull out. I have no doubt that at that time Dr Evans felt that this would actually put a stop to the programme, because he felt that we couldn't legitimately go on without a cardiologist. However, John Goodwin¹¹⁷ wrote to me and said, 'There are those of us within the cardiological community who would not like to see cardiac transplantation stopping in Britain at this time, and if you need any support with regard to assessing patients or help, I am prepared to come to Papworth, or you send the patients to the Hammersmith.' That support, coming at that critical moment was immensely important, because it allowed us to go on, feeling that we

¹¹⁶ Michael Petch was Consultant Cardiologist, Cambridgeshire Area Health Authority (Teaching), and East Anglian Regional Health Authority.

¹¹⁷ op. cit. note 86 above.

had the moral support we needed. We still had to run a service in which the surgeons did everything that cardiologists would normally do, such as right heart catheters, the cardiac biopsies and so on and in fact looking back on it, and I think this was actually a good thing, because not only did we learn to manage everything, but also got referrals from cardiologists who were more prepared to refer patients to a surgical transplant team than to another cardiologist associated with a surgical transplant team. And so I think there was, at that particular time of development, some merit in our being on our own. Now happily that didn't last, because in 1977 we got a cardiologist associated with the programme and that obviously has been of great benefit. But that was the big turning point, in 1980.

Wallwork: I remember, however, another side to that in that I was at Stanford at the time and Terence phoned up Shumway and said, 'Look, what do I do, my cardiologist has pulled out?' and Shumway said, 'Great, how did you make them do that? [Laughter] Carry on', which I thought was also equally good encouragement. I also remember at the time the Mayo Clinic decided that they wanted to do heart transplantation and they brought round a cardiologist, an immunologist, a respirologist, a bacteriologist, a surgeon and I don't know who else. They were going to do ward rounds by committee, and we explained to them that one person makes decisions and that's how the Stanford programme actually made it work and that's how I think Terence's programme made it work and at the end of the day one person made a decision. When there were more people at Papworth, we had a conflict of decision-making among consultants, so we made it the senior registrar was the only person who could write any orders on a patient. So it stopped all this bit-playing, which is what was the destruction of many transplant programmes – too many people, making too many silly decisions, without looking at the whole.

Treasure: I would like to bring Renée back. Before I do, you brought in mitral stenosis and you counted up the cases. Now it is interesting that in the 1920s there were ten mitral valve operations done, valvotomies and valvectomy, whatever you like. Two, one of Cutler's early ones and Souttar's in London, were long-term survivors, one for four years and one for about six or seven years. So there were two survivors out of ten. Between 1945 and 1948 also, and I have counted them up very carefully, there were ten operations done, before Brock started, by Bailey, Harken and Smithy,¹¹⁸ and there were only two survivors. It wasn't the numbers that changed the mood. Now, of course, there were a lot of

¹¹⁸ Dr Horace Smithy (1914–1948) was Associate Professor of Surgery at the Medical University of South Carolina, Charleston, South Carolina, and developed a valvotomy for aortic valvotomy in animals. He died from rheumatic aortic stenosis. See Smithy H G, Parker E F. (1947) Experimental aortic valvotomy. *Surgery, Gynecology and Obstetrics* 84: 625–628.

other things going on as well, but if you just count two out of ten, next time round it was two out of ten. I would like you to come back on the issue of the moratorium and to ask, ‘Do you think that behind all this there were big moods of the times, that the 1960s through the 1970s were moods of “technology can solve everything”?’ We are now in a mood where people are suspicious of doctors and suspicious of technological medicine, they are much more interested in diets and healthy living. I agree with them, I am not against that, but this background mood of the times, must also come into the changing views that the world takes of our practices.

Fox: I think that is relevant, but I also think there is an underlying dauntlessness in the early stages of a therapeutic innovation that is involved here. Take, for example, Dr Dwight Harken¹¹⁹ and Dr Charles Bailey.¹²⁰ Dr Bailey used up every single hospital in Philadelphia that he had available to him. At each hospital he did a mitral valve procedure and at each hospital he lost a patient very rapidly and all his privileges were taken away from him. Then in the very last hospital where he was permitted to operate, more by serendipity than experience, it would seem, he had his first success. Dr Harken, whom many of you know, had much the same kind of ‘you have got to believe’ personality and philosophy. In some ways those people who have what was referred to earlier today as ‘the courage to pioneer’, have to have a stronger belief in the face of that uncertainty than what is required when performing a more routine procedure. The moratorium is very relevant to this. This is illustrated by the literature on cyclosporin and its coming-in in the 1980s. The content analysis of the medical literature on cyclosporin in the English language that I have done suggests how this ‘you have to believe’ intrepidity contributed to the starting up again of cardiac transplantation. In very professional medical journals the language that was used about the coming-in of cyclosporin was evangelical. The literature was filled with ‘advent of cyclosporin’ phraseology and various terms like that. In the early reporting on cyclosporin, from the point of view of those people who had lived through the period of either having no immunosuppressive therapy at the beginning of the history of organ transplantation, as I saw at the Peter Bent Brigham Hospital, Boston, in 1954 where the world’s first successful human kidney transplants were done, or had to make do with the earlier forms of immunosuppressive therapy,

¹¹⁹ Dr Dwight Harken (1910–1993) was Chief of Thoracic Surgery at the Peter Bent Brigham Hospital, Boston, Massachusetts. See Harken D E, Ellis L B, Ware P F, Norman L R. (1948) The surgical treatment of mitral stenosis. *New England Journal of Medicine* 239: 801–809.

¹²⁰ Dr Charles Bailey (1910–1993) was Professor of Thoracic Surgery at the Hahnemann Hospital, Philadelphia, PA. For a description of his successful ‘commissurotomy’, a term first used by his cardiologist, Tom Durant, to describe Bailey’s operation, see Bailey C P. (1949) The surgical treatment of mitral stenosis. *Diseases of the Chest* 15: 377–397. Hurt R. (1996) *The History of Cardiothoracic Surgery: From early times*. New York: The Parthenon Publishing Group, 450.

this was received as a form of great deliverance. The literature, incidentally, recorded very little on actual or anticipated side-effects of cyclosporin, and went through a whole cycle in which you would have thought that an all-therapeutic therapy had finally been discovered – some kind of a drug that had no downside. The exception was Sir Roy Calne, who did write about the first eight cases on which he tried cyclosporin and I remember the phrase ‘cautious optimism’ that was a part of his article, because he saw and reported some side-effects. Then side-effects began to be reported by others, and at first were partly explained away by the fact that the proper dosage was not yet known. Finally, a more equilibrated reporting of the pluses and the minuses of cyclosporin ensued – at which point there was already in the wings tacrolimus,¹²¹ which was being hailed in much the same way that cyclosporin was. I personally had the experience of watching ACTH (adrenocorticotrophic hormone) and cortisone come in the same way,¹²² because of the years that I spent as a sociological participant–observer on the metabolic ward at the Peter Bent Brigham Hospital during the period 1951–54. One of the recurrent things about the moratorium that has to be understood is that great rush of enthusiasm and ‘we shall overcome’ kind of faith that therapeutic innovation often manifests in its early phases and the reaction to it that eventually comes afterwards.

One other thing, there has been some allusion made to the problem of finding donors. Of course, we are now in an era of organ transplantation where a good deal of the medical literature and not only the popular press talks about the major problem of organ transplantation being the shortage of organs, as if there were no other problems that superseded it, including the ever-present rejection reaction phenomenon which, though better managed, still is with us. A rather ironic situation at the present time emanates from the fact that so many organ transplants are being done that this contributes to the so-called shortage of donors. A phenomenon was mentioned earlier today about the supposedly strange reaction of one of the original donor relatives who wished to visit the recipient in whom the heart of his daughter beat. It is, in fact, a common

¹²¹ Tacrolimus (*Prograf*, Fujisawa) is an immunosuppressant used in liver and kidney transplant recipients. It has a similar action, and side-effects, to cyclosporin although not chemically related. See Knoll G, Bell R. (1999) Tacrolimus versus cyclosporin for immunosuppression in renal transplantation: Meta-analysis of randomised trials. *British Medical Journal* **318**: 1104–1107.

¹²² See Fox R C. (1959) *Experiment Perilous: Physicians and patients facing the unknown*. Glencoe, IL: The Free Press, 26–68. Reprinted in paperback by the University of Pennsylvania Press in 1974 and in 1998 with a new epilogue by Transaction Publishers, New Brunswick, NJ and London, UK.

reaction. That aspect of organ transplantation has been present since its inception and is very much with us today. Along with the numerous other factors, the anthropomorphic aspects of the meaning of giving and receiving organs may also contribute to the discrepancy between the number of organs one would like to have and the number of organs that one does have for transplantation.

English: Just a very brief point, Chairman, to say that the introduction of cyclosporin was actually one of the main bones of contention that Roy Calne and I had, because he, very understandably, took the view that he had had this early experience with it, which looked very promising in the kidney,¹²³ and that it would be desirable if we were going to start heart transplantation again, to start it with a new immunosuppressive agent, something that hadn't been used before. I took the rather more conservative view, that having set our sights on trying to achieve what Stanford had achieved with their protocol, that we should rather stick with that and let the problems of the side-effects of cyclosporin be sorted out by other teams first.

Treasure: It is an interesting point, as so often with these things, you have to recall that it wasn't that cyclosporin arrived and the clinicians said, 'OK we can start up again.' They had started up already and cyclosporin may well have been important in changing the figures, but it wasn't the key that opened the door.

Tyrrell: I was at a meeting about xenotransplantation with the pig, and with human recipients in mind, chaired by Professor Kennedy¹²⁴ and one of the points that came out and which I thought might be a useful way we have learnt the lesson was to say, 'Well we are not quite ready to start xenotransplantation yet, we will be soon, we will have to be strict about our criteria', but from then on we must expect the fact that there will be adverse effects and we must set things up so that we waste absolutely none of the information that we might garner on the way along, so that as soon as we can get to that point, we can make a rational benefit-risk assessment of where this new form of treatment is taking us. And I don't know whether it can be organized, but it would be wonderful if when xenotransplantation starts, because I think it may well do, there is right from the beginning some sort of collaboration between surgeons and surgical units which makes sure that all the information is built on and collected and the follow-up never stops while there is a chance of learning more for the patient.

¹²³ op. cit. note 96 above.

¹²⁴ op. cit. note 109 above.

Booth: I want to make two points. The first paper on cyclosporin in this country was written by Colin Green and Tony Allison in 1978 in the *Lancet*, about renal transplantation in the rabbit.¹²⁵ But going back to the point that you were making about the earlier years and why so few operations were done, I think if one looks at that in a historical context, one has to realize that the first thing that had to happen was the development of thoracic surgery and that derived from the thoracic surgeons who worked on tuberculosis. Bill Cleland,¹²⁶ for example, had all his original training as a physician, then became a surgeon of the chest and then moved on to the heart. So the opening up of the chest was crucial to the surgeon and the early operations were relatively simple ones, like tying a patient's ductus arteriosus, relieving constrictive pericarditis, and that sort of thing and then, we went on to the valves. But I don't think we should underestimate the very important significance of the cardiac catheter. Until the cardiac catheter came along, medical diagnosis of heart disease was pretty inexact.

Treasure: Well, of course, that's another witness seminar and unfortunately the witnesses aren't around, you are going back too far now, but we were simply drawing parallels about mitral stenosis which is one which is familiar to the two of us. I hope I didn't set off a hare running there.

Donald Ross: Well, I was going to come back to mitral stenosis if you don't mind, because it has been suggested that it was Cutler's self-imposed moratorium that stopped mitral stenosis.¹²⁷ I would believe that it was the cardiologists imposed the moratorium – Sir James Mackenzie and Sir Thomas Lewis – who were responsible for setting back the clock by saying that it's not the valve, it's the muscle.¹²⁸ I think I may say that that is the correct version.

Wallwork: I was going to comment on cyclosporin, not xenotransplantation, but I think you are both right. I think Terence, Magdi and a few others did start before cyclosporin started, but in fact the big explosion through the 1980s was entirely due to cyclosporin, not merely because the results were better, but also it was easier. And I remember I had two papers that never got published – the best

¹²⁵ Green C J, Allison A C. (1978) Extensive prolongation of rabbit kidney allograft survival after short-term cyclosporin-A treatment. *Lancet* i: 1182–1183.

¹²⁶ See biographical note, op. cit. note 85 above.

¹²⁷ op. cit. note 100 above.

¹²⁸ Mackenzie J. (1910) *Diseases of the Heart*. London: Hodder and Stoughton, 228. 'In chronic valvular affection the symptoms only arise where exhaustion of the heart muscle sets in. In organic lesions of the valves there may also be present advancing changes in the heart muscle.' See also op. cit. note 120 above, 444.

two papers, of course, that you ever write! The first was that I had monitored the number of phone calls that I got in the middle of the night after we started cyclosporin and it went down from about four or five to zero, which I thought was an amazing effect of this drug. And hence the fact that there was this important advent. The other was I wrote a paper about the early nephrotoxic effects of cyclosporin three months after we had started it and Roy [Calne] turned it down for publication, which I thought was...[Laughter]. And just seeing as this is a witness seminar I will just set the scene of what was happening at Cambridge when I came back.¹²⁹ I was interviewed by Sir Terence, who was not yet Sir Terence, and Sir Roy, who was not yet Sir Roy, and Roy turned up late for the interview having played squash and Terence was being very patient and Roy flashed his braces at me, which were yellow, and said, 'Well, what do you know about heart transplants and cyclosporin that we don't all know anyway?' and I said, 'Well, Professor Calne, my personal experience of heart transplantations is greater than the whole country's, and I know that cyclosporin works for heart transplants and you don't.' I don't know whether he voted for me or not!

Fox: I just wanted to make one brief comment about the xenotransplantation picture. At the Institute of Medicine's Workshop on Xenotransplantation, which ran parallel to the workshop sponsored by the Nuffield Foundation,¹³⁰ one of the most striking phenomena that took place at that workshop was that the transplant surgeons were very prudent about whether or not they thought the time had come to venture again to do xenotransplants. They were committed to starting again – eventually – but they felt that this was not the time to start up, because it was not going to work and they didn't want another public failure. The ardent people at the meeting about relaunching xenotransplants were the molecular biologists and the immunologists working on cells and tissues, not even on solid organs, at the animal level, who were very excited by their science and who were conflating cells and tissues with solid organs and who did not have clinical experience. They were reinforced by the presence of members of biotechnology companies in the audience, including prominent ones from the United Kingdom, particularly the company that is involved in the development of transgenic pigs. So there is a new configuration possibly on the horizon in the story of starting therapeutic innovations and moratoria upon them. I must say I

¹²⁹ *op. cit.* note 77 above.

¹³⁰ Institute of Medicine, Committee on Xenograft Transplantation: Ethical Issues and Public Policy. (1996) *Xenotransplantation: Science, ethics, and public policy*. Washington, DC: National Academy Press. Nuffield Council on Bioethics. (1996) *Animal-to-Human Transplants: The ethics of xenotransplantation*. London: Nuffield Council on Bioethics. The Chairman was Sir Patrick Nairne.

found it rather startling to see the transplant surgeons being conservative in this setting and the molecular biologists and immunologists filled with the hubristic conviction that we are ready to do xenotransplants right now.

Joseph: This is really just an aside, but I was fascinated to hear Terence mention John Goodwin¹³¹ intervening in the way that he did, I don't know how important it was to you (**Sir Terence** – Very.), but I know of one other example in which he has intervened in a similar way and I think we should pay a tribute to him.

English: It was hugely important.

Joseph: I think we should acknowledge him in this transcript.

Treasure: Just for these last ten minutes, I want to let people round up their ideas. I was going to ask Renée first, do you want to talk about the context of transplantation worldwide?

Fox: I don't think I need to any more, except that we keep getting back to the question of what individual teams were doing in particular countries in this historical period we are talking about, and confusing that a little bit with the larger picture of an aggregate phenomenon to which the individual decisions and actions of the particular teams we are talking about contributed. For example, all of what we are talking about belongs to a period of a great cardiac transplant boom that lasted for about two years, out of which very rapidly most teams involved fell out. Perhaps with different kinds of dynamics involved, with regard to particular teams in different national contexts, but there nevertheless is an aggregate phenomenon here and all the dates that have been cited for example are not just relevant to the United Kingdom or to the particular teams represented here today, but fit into a larger picture that can be characterized as part of a more international phenomenon.

Treasure: Donald [Ross], you thought it was like sheep. Would you stick with that comment?

Donald Ross: It was like a movement of sheep and it involved, as I think you have pointed out, some good teams but many were just there for national prestige, not really teams at all, individual surgeons. We had a meeting in Cape

¹³¹ See biographical note, op. cit. note 86 above.

Town where the government looked after us very well, took us up Table Mountain, and flew us around in helicopters, and whatnot, and most of the people had done one transplant. But yes, it was a movement of sheep.

Gilston: It's perhaps not strictly relevant to this discussion, Chairman, but I think there's been a symbiotic relationship between medicine and cardiac surgery in that intensive care was given a tremendous boost by the advent of cardiac surgery and in turn intensive care now is involved in the management of these patients, whereas in the early days they were just respiratory units, now they are multi-organ failure units, and I think their importance in this context can't be ignored.

Treasure: Sir Terence I wonder if you would say a few words and perhaps bring it to a close?

English: Well, I would like to make three unconnected comments, because I think they are relevant to the overall subject this afternoon.

The first one goes back to the media and the press and their responsibilities and I think the television programmes that *Panorama* mounted on brain death at the end of 1980 was about the most unethical and irresponsible bit of TV journalism that there's ever been in this country.¹³² What was disturbing was that they knew that the individuals they filmed, who were largely from America, did not have anything to do with trying to meet the British criteria for brain death and yet it was so subtly done that it created doubt not only amongst the public, but also amongst the medical profession, and to me, that was the epitome of unethical TV journalism. It did huge damage in terms of referrals of donors for kidney transplants and heart transplants for about six months.

Secondly, I think something we haven't touched on, is the impact that a transplant programme has on the other hospital services that are being delivered in that institution and it's inevitable that this should be so. Here, the two hospitals at Harefield and Papworth had a special situation in that we were, and are, single-specialty hospitals and to that end we weren't competing with orthopaedics, general surgery, general medicine, either for beds or resources, or

¹³² The BBC's *Panorama* programme, 'Transplants: Are the donors really dead?', was transmitted on Monday, 13 October 1980. A second programme, scheduled for 24 November, was cancelled following a dispute between the programme controllers and the Conference of Medical Royal Colleges over editorial control. See Anon. (1980) Notes and News: Brain Death, the doctors' case. *Lancet* ii: 1205. For an analysis of transplants registered following the programme, see Bradley B A, Brooman P M. (1980) *Panorama's* lost transplants. *Lancet* ii: 1258–1259.

anything else. And we could also perhaps get the team, the key individuals within the hospital not just the consultant staff but all the medical technicians and everybody else, actually interested in seeing the programme going ahead without divided loyalties. I think that was very important, both for Papworth and Harefield.

And then, thirdly, I stopped at the time when Papworth and Harefield were designated as supra-regional services, and this I think is something that the Department of Health can be proud of. I see that Geoffrey Rivett has left the meeting unfortunately, but it really was much admired by other countries as to how Britain handled this new development of cardiac transplantation and controlled the establishment of new centres as it was based on the premise that when the two units had reached more or less their full capacity then an additional unit could be approved, preferably in a different part of the country, but they would have to meet certain defined criteria by the Department before funding was forthcoming and then designation carried continuing funding. And in this way over the decade the units in Newcastle, St George's, Manchester, Birmingham, could be planned in a rational way, so that they were doing a reasonable volume, or had the potential to do a good volume of work, rather than as happened in the United States, where you had 160 units, none of them really doing enough to get the experience that is so important. That is something which the Department can be proud of, and I was very sad when two years ago the Department decided to de-designate cardiac transplantation for supra-regional funding because it was not consistent with the new reformed Health Service, which sought contracts between purchasers and providers.¹³³ I am quite sure that this is going to have a damaging effect, but this is something that we are going to have to live with.

Treasure: Thank you very much indeed, Sir Terence. And it remains to say thank you to everybody. I am very, very grateful to those who were witnesses of the events who came and, of course, Mr Donald Ross, Professor Donald Longmore, and Sir Keith Ross, but cardiac surgery is a team effort and heart

¹³³ Following a review by the Chief Medical Officer, Sir Kenneth Calman, a new expert group was established to advise the Minister of Health on purchasing, taking over from the Supra-regional Services Advisory Group on 1 April 1996. See Beecham L. (1996) *Medicopolitical Digest: Supra-regional Services have new advisers. British Medical Journal* 312: 316. See National Specialist Commissioning Advisory Group. (1998) *Annual Report 1996-97*. London: Department of Health. Figures are given for transplants performed at the designated centres for heart transplantation from 1993/94 to 1996/97: Harefield Hospital (in association with the Royal Brompton Hospital); the Northern General Hospital, Sheffield; Papworth Hospital, Cambridge; the Wythenshawe Hospital, Manchester; the Hospital for Sick Children (Great Ormond Street), London; St George's Hospital, London; the Freeman Hospital, Newcastle; and University Hospital, Birmingham.

transplantation a team effort more than any other form of cardiac surgery. So to have the anaesthetists, the people who were registrars at the time, those who were housemen, chemical pathologists, and immunologists, and so on around us, has been absolutely fascinating and I have enjoyed it a great deal. I know from my phone calls to you, it stirred up memories which weren't 100 per cent happy, nevertheless I hope this has been an enjoyable reunion for some of those teams and an opportunity to reflect on it in a positive way and to contribute to a bit of history. I would also like to thank the Wellcome Institute and my colleagues on the Twentieth Century Group for all the work they've put in with us trying to put this together in its planning phases. So thank you all very much for coming.

Joseph: Sorry, Tom, you are supposed to have finished, and I apologize, but I would like to pay a special tribute to Donald Ross, who was an inspiring person to work for, who got cardiac transplants going in this country and who generated both Terence and Magdi. I think we should thank him especially. [Applause]

Treasure: Finally, just so that you know why we have to have anaesthetists around us of the calibre of Alan Gilston, he wants to give you a quote and then we will go for a drink.

Gilston: First of all, Mr Chairman, I would like to congratulate you for this excellent meeting. And the second thing is that I collect books of aphorisms and quotations and this afternoon, just before the meeting I picked up the *Oxford Dictionary of Humorous Quotations* and I thought you might like to hear this one.

When organs have been transplanted
And the new ones made happy to lodge in us,
Let us pray one wish be granted –
We retain our zones erogenous.¹³⁴

¹³⁴ Harburg E Y. (1965) Seated one day at the organ. In Sherrin N. (ed.) (1995) *The Oxford Dictionary of Humorous Quotations*. Oxford: Oxford University Press, quote on page 230.

Early Heart Transplant Surgery in the UK

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