



The Voice of Transplantation in the UK

The History of the BTS



A British Transplantation Society Publication

James F Douglas - 2015

(updating the version compiled by
Professor Mary G McGeown in 2001
and revised in 2007)

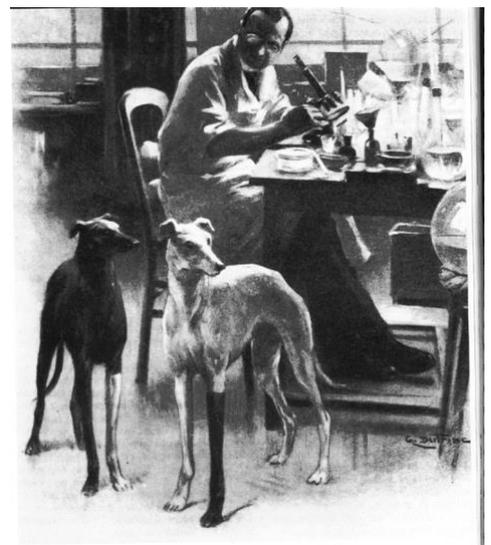


Clinical transplantation is today firmly established and the science underpinning it is fairly well understood.

This was not the situation in 1971 when the British Transplantation Society (BTS) was founded. Indeed, it was the need for fuller understanding of the rejection process and the ambition to find better and safer ways to overcome it that helped bring the society into existence. The many developments since 1971 are fully recorded in the medical and scientific literature and need not be described in detail here, although they are central to, and often resulted from, the work of the BTS and its sister organisations. But the early history of transplantation deserves more attention for several reasons. First, it is inherently interesting. Second, although some excellent accounts exist, these are not always available in books on transplantation. Third, it should prove instructive to younger BTS members, some of whom were not yet alive in the pioneering days. Fourth, it provides an explanatory background to the birth of the Society.

The concept that a diseased body part might be replaced by a healthy organ from a recently dead person was already present in the Middle Ages. Paintings from the fifteenth century record the legend of Saints Cosmas and Damian. The saints, having removed the cancerous leg from a sleeping man, are shown replacing it with a healthy one transplanted from a dead man. Nearer to our own time, in 1902, Ullman, in Vienna, found that a dog kidney, autotransplanted to the neck, produced urine, as did dog-to-dog and even dog-to-goat graftings.

In 1905, in Boston, Alexis Carrel repeated Ullman's experiments, but found that, after producing urine for a few days, the kidneys failed. Nevertheless, his extensive work on surgical procedures, notably vascular suturing, laid the groundwork for future operative techniques and won him the Nobel Prize in 1912. Jaboulay, in Lyon, reported two unsuccessful human xenografts in 1906 for chronic renal failure, indicating that the immunological barrier was not yet recognised. It was Carl Williamson, in the USA, in 1923, who first examined a failed kidney transplant, described its histology and introduced the term 'rejection'. In 1933, in the Ukraine, Voronoy made

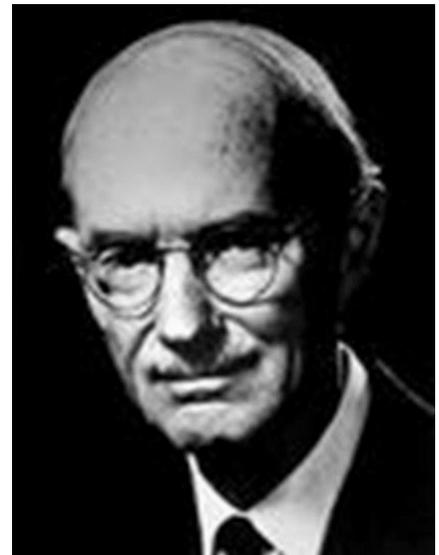


Alexis Carrel: Pioneer of Transplantation

unsuccessful attempts to transplant kidneys between human subjects. It seemed then that, while the surgical challenges of kidney transplantation had been overcome, the problem of rejection was insuperable.

Events external to surgery now influenced progress. During the Second World War, the bombing of large cities and other catastrophes of conflict led to many cases of multiple injury. Thanks to improved medical management, casualties with extensive burns, who would formerly have died from loss of plasma, fluid and electrolytes, or from infection, now often initially survived, albeit with large areas devoid of skin. Unfortunately, skin autografts, despite attempts to maximise the use of available tissue, were often insufficient. These cases not only stimulated research into methods of tissue replacement, but also intensified the need to understand the process of tissue rejection. Already, even before the First World War, interest in the future discipline of immunology had begun. In 1903, Jensen reported that tumour cells injected into mice grew better in some than in others. If such an injected tumour resolved, re-injection of identical tumour cells into the same mouse failed to produce another growth.

In 1936, George Davis Snell, working in the Jackson Laboratory in Maine, began to study the behaviour of transplanted tumours. He developed highly inbred strains of mice over a decade of sibling mating. Within each strain, every mouse had the same genetic constitution. He showed that transplanted tumours grew in all mice of the same strain, but were rejected by all other strains. These tumour cells would grow only if the donor and recipient shared certain dominant genes. If not, they were destroyed by host ("killer") lymphocytes. Snell realized that similar principles must also regulate growth of normal tissue and began to identify the relevant genes. He called them "histocompatibility genes", a title which he modestly attributed to his neighbour across the hall. He found at least 80 genes of differing strengths and named the strongest the H2 gene. Meanwhile, in London, in 1936 and 1937, Peter Gorer had identified four leucocyte antigens in the mouse, using heterologous sera, which he designated I, II, III and IV. One of the genes segregated with susceptibility and resistance to a transplantable



George Davis Snell: Discovered the HLA antigen system.

tumour. In 1946 he went to Bar Harbour, where, working with Snell's inbred mice, he showed that leucocyte antigen II corresponded to Snell's locus, the H2 gene.

Although skin taken from a woman's thigh had been used successfully to reconstruct her nose as early as 1823, and similar grafts had been used in India for hundreds of years, later workers seemed unaware of the difference between autografts and allografts. Lexer stated in 1911 that skin grafts invariably failed, even between parent and child, and dismissed reports of past successes as fables. However, during the 1940s, Billingham, Medawar and Brent, in London, studied skin transplantation in rabbits. Medawar's publications on skin autografts and allografts appeared in 1944. In a joint study with Snell, he showed that a graft of foreign skin into an unborn mouse would survive. This was the basis for later concepts of tolerance and enhancement. Medawar also discovered that, in rabbits, a second graft from an initial donor underwent accelerated rejection. Later, in the 1950s, Dempster found an identical effect in dogs and several groups showed that human skin grafts behaved in the same way. Blood group compatibility had once been considered important in skin grafting, but, from the 1920s, it had been known that it did not, in fact, ensure graft survival. Following the demonstration, by Medawar's group, that non-identical cattle twins, which shared a foetal circulation, mutually accepted skin grafts after birth, the importance of Snell and Gorer's histocompatibility antigens in transplantation was realised. Similar effects were found in mice injected with leucocytes in the pre- and post-natal period. Even more important was the discovery that tolerance could be induced. This had not been predicted by Medawar. He had been invited to distinguish identical from non-identical cattle twins by the skin grafting technique. Instead, he went on to develop his seminal studies in acquired tolerance.

The enormous casualty lists of the Second War had focused attention, not only on skin destruction, but also on loss of renal function, which previously had been poorly understood. Many severely wounded patients often survived the initial trauma, only to die later from acute oliguric renal failure associated with haemo- and myoglobinuria. In victims of bomb compression injury with muscular damage, the condition known as the 'crush syndrome' and had a mortality of over 90 per cent. All previous attempts to replace renal function by dialysis had failed. But in 1944, in the Netherlands, Willem Kolff reported the successful treatment of acute renal failure by means of his 'artificial kidney'. He had shown, for the first time, that many cases of acute renal failure were self-reversing, if the patient could be kept alive by haemodialysis until the kidneys recovered. Interest in dialysis began

to revive. After the war, Kolff gave artificial kidneys to the Hammersmith Hospital in London, Mount Sinai in New York, and the Royal Victoria Hospital in Montreal, where they were used with some success. He also gave one to Amsterdam; but it was never used. In 1948 Bywaters and Joekes published a series of twelve patients treated by haemodialysis at the Hammersmith Hospital. These events led to the creation of the Renal Association in 1952. Founder members included Robert Platt and Arthur Ellis, interested mainly in nephritis, Clifford Wilson, working on hypertension and diabetes, and Robert McCance, Douglas Black and Malcolm Milne, investigating electrolyte problems.

The belief grew that dialysis could also be used to treat irreversible chronic renal failure. This re-ignited hopes for transplantation, if only the major obstacle - rejection - could be overcome. Hufnagel, Hume and Landsteiner, working on acute renal failure in Boston, had shown that short-term human allograft function was achievable. There was increasing awareness that immune mechanisms were responsible for rejection, as suggested by the dog transplants of Simonson in Denmark and Dempster in London. Hamburger, Kuss and others, in Paris, using a pelvic site, persuaded clinical allografts to survive for up to three weeks, after which rejection destroyed them. Among several unsuccessful clinical series in the early 1950s, those of David Hume, in Boston, were the most instructive. Hume rightly predicted the importance of blood group compatibility and used steroids against rejection. He realised the need for pre- and post-operative management with haemodialysis and reported the first case of disease recurrence in the transplanted kidney. To the surprise of the modern reader, he favoured a femoral site. However, contemporary medical opinion often dismissed these results as insufficient and premature, asserting that successful transplantation would be impossible unless a state of permanent immune tolerance could be induced. Some considered that transplanted organs would be non-viable on physiological grounds, also believing that the pathological and clinical effects of terminal uraemia were in any case irreversible.

The first successful transplants

In 1954, Murray and Merrill, in Boston, performed the first successful live human kidney transplant, between identical twins and with long-term survival. This clinical triumph, for which Murray later received the Nobel Prize, confirmed the technical efficacy of transplantation and its ability to reverse the effects of chronic uraemia. Over the next few years



*Portrait of Joe Murray by
Sir Roy Calne*

successful identical twin transplants were undertaken in a number of centres, including the UK's first, performed in 1960 by Woodruff, in Edinburgh. But deviation from the identical relationship, even if slight, invariably led to rejection. Nevertheless, since transplants between close relations usually survived longer than those between unrelated subjects, tests were devised in the hope of identifying suitable donor recipient pairs, including the third party skin graft and the lymphocyte transfer test - these did not prove useful when applied to patients and their families. Attempts were made to prevent rejection of the graft by whole body irradiation. It was used with allograft bone marrow infusion in both Paris and Boston, but proved too difficult to control. However, sub-lethal radiation achieved modest success in sibling grafts. A search began for immunosuppressive drugs with which it might be combined. In 1959, Schwartz and Dameshek discovered that the purine analogue 6-mercaptopurine (6-MP) impaired the ability of rabbits to produce antibodies in response to injected foreign protein. Kidney grafts in dogs were protected by 6-MP, despite considerable toxicity. In 1960 Kuss and Legrain, using 6-MP together with irradiation, reported long-term survival of a kidney donated by the recipient's brother-in-law. In the same year, Goodwin successfully used steroids to control acute rejection. But a high incidence of fatal infection, caused by the loss of immune competence resulting from the need to reverse the rejection process, still deterred optimism. These two formidable 'enemies' - rejection and infection - were to dominate the clinical scene for many years.

The first well-documented clinical kidney transplant in the UK was carried out in 1955 by Rob and Dempster at St Mary's Hospital on a case of acute renal failure (following septic abortion). It failed; but from 1959 onwards Peart and colleagues achieved modest graft survivals of 31 to 80 days in some recipients. At Leeds General Infirmary, Raper, supported by Parsons, started to do 'cadaver' (now 'deceased') donor transplants in the same year. One recipient survived for eight months. Previously, in 1957, John Hopewell ([read his excellent Memoir on the BTS website](#)) had set up a renal unit at the Royal Free Hospital 1961, specifically for the treatment of chronic renal failure.

He was joined in 1958 by Roy Calne, whom he helped to begin research at the Royal College of Surgeons experimental farm (Buckston Browne) at Downe, in Kent. This work, which used 6-MP for a series of canine allografts, encouraged them to attempt a number of clinical transplants.



Sir Roy Calne

Of these, one recipient (from a living related donor) survived for seven weeks. In 1960 Calne moved to Boston to work with Murray's group. After he had made contact with Hitchings and Elion at Burroughs Wellcome, in New York, they had given him several compounds to study, including azathioprine, which was a derivative of 6-MP, and, in his opinion, only slightly superior to it. However, he found that it prevented rejection in dogs and was somewhat less toxic. In 1962, in conjunction with Murray, he reported its successful use for a deceased donor transplant in which the kidney had been taken post-mortem from a patient who had died during open-heart surgery. Despite several rejection crises, the organ supported the recipient for two years, after which he received a second transplant.

Calne and Murray's successful use of a deceased donor organ opened new doors for transplantation. During the 1960s, surgeons in the USA and Britain began to transplant these kidneys, using azathioprine and corticosteroids. In most centres, especially in the USA, there remained a preference for living related donors, but a few used deceased donor kidneys almost exclusively. They were helped by the emerging concept of 'brain death', or '*coma depasse*', as defined by Mollaret and Goulon in 1959 and first applied in the Necker hospital in Paris. This allowed assisted ventilation to be withdrawn from deceased donors in an ethical manner. Legal uncertainties regarding the new practices were partly resolved by the Human Tissue Act 1961, which later became the authority for the 'Organ Donor Card'. The development of cold organ perfusion solutions, such as Collins's 'intracellular' preparation in 1969 (which prolonged the viability of a donated kidney for 24 hours or more) was another essential step. With more time available, and with maintenance haemodialysis units appearing in many medical centres, planned deceased donor renal transplants were becoming practicable, as was the elective selection of recipients on the basis of blood group and tissue typing compatibility.

Tissue typing had been introduced into clinical practice in the early 1960s, following Jean Dausset's discovery of the MAC antigen, later re-named HLA-2. In 1965 van Rood and van Leeuwen, in the Netherlands, and Terasaki's group, in the USA, both proposed leucocyte HLA antigen matching as tests for selection, based on the knowledge that these antigens reside in the leucocyte cell membrane and that HLA-A and HLA-B had been identified as part of the major histocompatibility complex in man. With the discovery that some pregnancies lead to formation of specific anti-HLA antibodies, a source of reagents for matching recipients and prospective donors became available. The need to conserve

precious monospecific sera led to the introduction of the microleucocytotoxicity test by Terasaki and McClelland in 1964. Another method was the mixed lymphocyte culture test (Bach and Voynow, 1966). This was performed by mixing the lymphocytes of the recipient (the responding cells) with those of the proposed donor (the stimulating cells), which had been pre-treated with mitomycin-C to make them inert. The mixed lymphocytes were then incubated with radioactive thymidine, the degree of uptake providing an assay. As the test took at least three days to perform, it was effectively limited to living donors.

The late 1960s and early 1970s saw progress in both forms of renal transplantation. Azathioprine was by no means risk-free, but, when combined, in lower dose, with steroids, it became safer. Success rates improved, but there were many disappointments, due to the mortality of 'high-dose' steroid maintenance regimes, which had to be further increased in the event of acute rejection. The clinical use of a polyclonal antilymphocyte serum (ALS) by Starzl, in 1967, was a step towards more selective methods. Its potential in organ grafting had first been investigated by Michael Woodruff, in Edinburgh.

In 1968, McGeown and colleagues devised the 'Belfast Regime', intended to reduce mortality by use of low dose maintenance steroids, intensive isolation methods and a commitment to return to dialysis all recipients whose grafts had failed. This regime, which included bilateral nephrectomy in many patients, as well as much pre-transplant blood transfusion, had by 1975 achieved five-year cumulative graft survival rates approaching eighty percent, with a strikingly low infective mortality. Such improved clinical practice showed that high dose regimes were not essential to success and pointed the way towards transplantation as a routine procedure. Morris, in Oxford, developed a similarly successful protocol in the mid 1970s. The discovery that minimal immunosuppression could keep a graft in good condition over a long period of time encouraged the later development of regimes designed to induce a clinical state of 'prope'-tolerance.

The kidney had clear advantages as a transplantable body part. First, since a single kidney sufficed to maintain health in a live donor, the second could be removed for transplantation without excessive risk. Second, provided urinary drainage could be established, its placement in the recipient was relatively straightforward and permitted some flexibility. Third, the availability of dialysis reduced clinical urgency, allowed pre- and post-operative support and provided an escape route in the event of failure. Nevertheless, attempts to transplant other organs had been made. Skin and corneal grafts were in a

separate, relatively well-trying category, due to their lesser dependence on tissue compatibility.

Tom Starzl, in Denver, had shown the feasibility of liver transplantation by 1963. He had some early success, using azathioprine, actinomycin C and steroids, but survival was disappointing, mainly because of septicaemia and other systemic infections related to complications of graft biliary drainage. Lung, pancreas and intestinal transplantation had achieved even less. In 1968 the first liver transplant outside of the USA was performed by Calne, in Cambridge, but liver transplantation remained for some time largely experimental, with formidable morbidity and mortality.

In 1967, in Capetown, Christiaan Barnard performed the first technically successful heart transplant, using techniques pioneered by Norman Shumway and Richard Lower in the USA. The death of the recipient after nineteen days (from infection) and the poor results of a subsequent planet-wide cardiac



Christiaan Barnard performed the first technically successful heart transplant

transplant frenzy (to paraphrase Rene Kuss) which produced 60% failure in less than a year, overshadowed the few long-term successes, which included those of Lower and Lepley in the USA, and Henri and Monties, in Marseille.



Image: courtesy of Dr Chris Winearls of the Oxford Transplant Unit

Transplant Unit and Renal Ward opened by Sir Peter Medawar August 21 1977

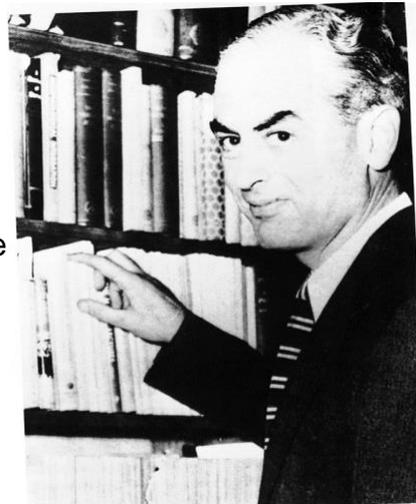
The birth of the British Transplantation Society (BTS)

By the start of the 1970s, although hope for progress with other major organs remained high, only kidney transplantation, despite many difficulties, had become established as a clinically effective treatment for end-stage renal failure. By 1971, doctors in the London area (mainly with a renal interest) were meeting regularly to share experiences and discuss problems, especially in the field of tissue typing. These informal meetings, organised by John Hopewell from the Royal Free Hospital, developed into the London Transplant Club. Surgeons began to co-operate by sharing deceased donor kidneys, those centres not actively engaged in transplantation contributing suitable patients with near-terminal renal failure. Methods for perfusion and rapid cooling of kidneys were well established and, within the London area, the transfer of organs between donor and recipient centres, in a sterile slush of preservation fluid, was easily arranged. In the following year (1972) Belfast joined the Club, contributing and receiving many of its kidneys by emergency flights of the St John's Ambulance Air Wing.

Although some progress had been made in HLA typing, most transplantation was based on ABO matching or compatibility. But, in the London area, several immunologists (among them Hilliard Festenstein, Richard Batchelor, and Walter Bodmer) were actively working on the leucocyte antigens. Their material was frequently reported to the British Society of Immunology (BSI). The international Transplantation Society had emerged some years earlier from meetings on tissue typing and human allografts at the New York Academy of Sciences; and a first International Congress of Transplantation had been held in 1966. At a meeting of the London Transplant Club on 28th September 1971, the need for a similar organization in the UK was discussed. John Hopewell received many supportive letters, and sent a circular letter to those he thought might be interested in forming a society. Support was widespread, from physicians as well as from surgeons and immunologists, although some dissenting voices were heard - one writer considered that 'British Association of Organ Replacement' would be a less 'emotive' title. After further discussion at a meeting of the BSI on 20th October 1971, Roy Calne wrote to John Hopewell that its members, almost all immunologists (and including Hilliard Festenstein, Richard Batchelor, and Walter Bodmer) wished to set up a combined transplantation and immunology society. Upon suggestions that this new society's meetings (or some of them) might precede or follow those of the immunological society, which drew attendance from all over the British Isles and Europe, the BSI formed an *ad hoc* committee to plan two,

mainly immunological, meetings per year, plus two more, possibly in the provinces, which would be clinically orientated.

An inaugural meeting was held at the Royal Free Hospital, London, on 12th April, 1972, at which about 80 persons were present. Professor Sir Peter Medawar was invited to take the chair. A steering committee was set up, with Sir Peter as chairman, which included the members of the *ad hoc* committee, the BSI having two representatives. The meeting also established the Constitution Committee, and elected office bearers and committee members. Sir Peter was elected Chairman, Dr Leslie Brent General Secretary, Mr Anthony Barnes Meetings Secretary, and Mr John Hopewell Treasurer.



Sir Peter Medawar: First Chairman of the BTS

It was eventually decided that the spring and autumn meetings should be associated with the BSI, and that there should be at least one other meeting, preferably outside London, each year. The Wellcome Foundation offered a meeting place and hospitality. The BSI provided temporary funds, as well as the use of its secretariat. Seven papers were presented at the meeting, separated into scientific and clinical sessions. Appropriately, Sir Peter Medawar led on 'The contribution of transplantation biology to immunology and experimental biology'. Further papers covered rejection of the mouse small intestine, polymorphisms at the MLR locus in pigs and the human foetus as an allograft. Clinical papers discussed the leucocyte migration test in the diagnosis of early rejection, the outcome of 100 renal transplants and (from the team of Chisholm, Shackman and Peters) the concept of 'transplantation without dialysis'.

Professor Pierre Grabar was elected the first Senior Member. For the first three months, founder membership applications required approval by the Committee. At this time there were 202 such members, including one Fellow of the Institute of Laboratory Technicians. New members were to be proposed and seconded by existing members, scrutinized by the Committee and elected at the next Annual General Meeting of the Society. At the second meeting, on 18th October, 1972, provision was made for honorary membership to be given to distinguished individuals who had contributed significantly to knowledge of transplantation. In 1972, George Davis Snell was elected the first Honorary Member. In

1980, he shared the Nobel Prize for Physiology with Baruj Benacerraf and Jean Dausset, both also later elected Honorary Members.

The first constitution laid out three main aims for the Society. It would

- Advance the study of the biological and clinical problems of tissue and organ transplantation;
- Facilitate contact between persons interested in transplantation;
- Make new knowledge available to any person for the good of the community. It might also
- Concern itself with the social implications of transplantation.

Although later constitutions, for unclear reasons, transformed the Chairman into a President and the Committee into a Council, these original aims remain essentially the same.

Until the end of the 1970s, three meetings were held annually. As it transpired, the spring meeting came to be in the provinces, the others in London. About half the London meetings were held in the Wellcome Foundation, the rest in hospitals, the Royal Free Hospital often offering facilities. Combined meetings were held in Paris in 1978 and in Leiden in 1981, with the French and the Dutch Transplantation Societies respectively. From 1981, two meetings were held each year, either in hospitals or at the Royal Colleges of Physicians or Surgeons. These were two-day meetings consisting of a series of symposia, with presentations chosen from abstracts submitted by members on subjects of special interest. Each meeting included at least one invited lecture by an eminent authority on some aspect of transplantation or immunology.

In 1998 a single three-day Annual Congress was introduced by the Council, the first being held in Dublin. It proved popular. The Congress now consists of both plenary and parallel sessions, to allow space for general and specialised subjects. Clinical Transplantation, Immunology and Basic Science are always included. As far as possible, all aspects of transplantation receive regular representation. Most sessions contain lectures by invited speakers, often Society members, who are domestic or international leaders in their fields. In keeping with the Society's objectives, it is usual to include sessions on organ donation and procurement, transplant co-ordination, ethics and patient-related issues.

A plenary session is reserved for young members competing for the Medawar Medal, awarded to perpetuate the memory of Sir Peter Medawar, Nobel Laureate and founder BTS Chairman. It was first presented in 1990. In 2007, because of the difficulties of comparing work in different disciplines, it was decided that two medals would be awarded annually, for clinical and basic science presentations respectively. In the light of this decision it is interesting to recall the exhortation of Meetings Secretary Roger Blamey before the autumn meeting of 1978 :- 'Speakers are reminded both of the need for papers in complex subjects to be understood by members in all disciplines relating to transplantation and of the need for clear slides. Chairmen will be encouraged to rebuke, halt and, if necessary, précis speakers'. How far this counsel has been followed is a matter of opinion; but it has a strong mandate in the Society's expressed constitutional aims. Congress presentations are selected from abstracts by an abstract committee, which also selects an increasing number of poster presentations. Sessions, days and meetings have at times been shared with other interested societies. Pre-Congress symposia were introduced in 2006, a move which emphasises the importance of the single meeting, as well as the diversity of subjects and specialties which exist to promote transplantation. All members can attend the Annual General Meeting during the Congress, and a Council meeting is also held. Members and other participants have the opportunity to meet and converse on what they will at company exhibitions and social events. In addition to the main Congress, regular educational 'Summer Schools', at rotating venues, were held over many years, although these have been replaced by more occasional 'subject-specific' meetings.



Image by Sir Roy Calne

Working groups and temporary sub-committees have been set up by the Society on various occasions to investigate particular issues or resolve problems. For example, in

1980, the so-called 'centre effect' (the emergence of significant variations in renal transplant outcome between centres) led to an investigation and visitations by a BTS team, dubbed the 'Three Wise Men'. The Wise Men considered the effect to be caused by differing incidences of acute rejection and death with functioning kidney. Pre-transplant blood transfusion, the introduction of cyclosporin and strict post-operative management policies were associated with the more successful centres, although these factors did not fully explain the effect. The Wise Men reported at the end of the azathioprine era. A second investigation, in 1989-90, still showed unexplained variation, but, with near-universal use of cyclosporin, outcomes had improved in most centres.

At first, working groups were always set up by the BTS Committee, but the Society now encourages individual members to set up forums for specific purposes. These have the support of the BTS, provided they comply with certain rules and report to the Council. Several currently exist, a recent re-creation being the Carrel club, which concerns itself with surgical issues.

Several sub-committees have become permanent. In 1986, a Supervisory Committee on Organ Transplantation was created, following publication by the BTS of its 'Recommendations concerning the use of living unrelated donors in the United Kingdom'. The 1980s were a time of improving transplant outcomes. Many were becoming aware that even poorly-matched live kidney donations could produce excellent results, with a quality and duration of survival unobtainable by dialysis, and that a pool of potential donors might be found, through 'market forces', to eliminate the prolonged, possibly fruitless, wait for a deceased donor kidney. The Society was concerned that all live donation should follow ethical principles, be non-exploitative and remain wholly altruistic. The Supervisory Committee acted as an informal referee in such cases, some of which raised complex issues of motive, relationship and medical authority. Representative members lobbied the Department of Health, the General Medical Council and the British Medical Association, advocating compulsory registration of live donations. Although the USA had passed a transplant law in 1984, Westminster was slow to respond until the exposure of unethical practices in a London clinic in 1989 prompted the rapid passage of the Human Organs Transplant (HOT) Act 1989. The HOT Act put some of the Committee's recommendations into effect, but, in addition, transferred the decision on unrelated live donations to a statutory regulatory body (ULTRA).

In retrospect, the Supervisory Committee's recommendations (published in the British Medical Journal in 1986) appear very cautious. The committee preferred deceased to living donation, which it considered to be justifiable only in exceptional circumstances. Live unrelated donation was deemed acceptable only at the request of spouses or very close friends, after at least six months on the cadaver transplant waiting list. In 1987, the committee appeared to approve a Council of Europe ruling that 'removal of organs from living donors should be restricted and, where possible, gradually eliminated'. This is far removed from the Society's present guidelines on live donor transplantation (2012) which now recommend all forms of live kidney donation (including paired, pooled and non-directed altruistic donations), as a treatment of choice, on the grounds of its superior outcome and ability to pre-empt the need for dialysis in renal failure. This reversal of opinion stems, in part, from clinical experience based on scientific advances, but also reflects changes in ethical emphasis brought about by the successful outcomes themselves, as well as by the continued widespread shortage of donor organs.

After 1989 the Supervisory Committee underwent a metamorphosis into the present Ethics Committee, which has an important role in the Society. The evolution of transplantation raises complex ethical and legal questions created by new clinical and scientific advances and this process is likely to continue. The Ethics Committee is responsible for considering such issues and assisting the Society to have an agreed position on them. They are often controversial, engendering much debate at Congress ethics sessions. Since 2010, this has been enhanced by the annual Hoffenberg Lecture, inaugurated in honour of Professor Sir Raymond ('Bill') Hoffenberg (1923-2007), a former President of the Royal College of Physicians, whose many interests included ethical problems in transplantation. The Committee, on behalf of the BTS, has produced position statements and comments on many of these problems, which are available on the BTS website. It has also arranged a series of Winter Ethics Forums at which important contemporary ethical issues can be presented and debated.

The Standards Committee appeared in 1998, at a time when outcomes were uniformly improving, with little significant variation between centres. Nevertheless, partly in response to discrepancies in outcomes such as those revealed by the inquiry into children's heart surgery at Bristol Royal Infirmary, there was concern that best practice in transplantation should be seen to be uniform throughout the country. In addition, a government-supported campaign for 'evidence-based medicine' was underway which, although somewhat

invidious to a society dedicated to scientifically-based progress, was in keeping with public opinion, which now perceived transplantation as an established, rather than an exceptional, treatment. Members in general welcomed the drawing up of BTS guidelines, both as a source of reliable information and as a form of protection against criticism. The first guidelines, since updated, appeared in 1998 and have been followed by many more. Clear, comprehensive and readily available on the BTS website, they have been well received, a tribute to the immense amount of work done by this committee, sometimes in association with other societies. It is important to realize that, while authoritative, guidelines are only a *guide* to best practice, do not have the force of law, cannot be a substitute for individualized treatment and are liable to become out-of-date with time. It is to be hoped that this helpful body of informed consensus will never become a template for unreasoning conformity.

The Transplant Training and Education Committee (TTEC) reports regularly to the BTS Council. One of its main functions has been to advise on the career structures of young transplant surgeons and to promote recruitment into the discipline. Transplant surgery at first developed in a piecemeal fashion, often as a result of the individual efforts and enthusiasm of researchers and their assistants. These arrangements could not survive the modern expansion of transplantation and its extension to multiple organs. Some transplantation developed as an extension of existing specialties, such as cardiac and thoracic surgery, but other transplanters had more diverse backgrounds. Despite clinical and academic attractions, a crisis in recruitment emerged during the 1990s and early 2000s, whose resolution involved input from the TTEC. More recently, training in transplant nephrology and other non-surgical fields has become an issue. Since 2014, the TTEC meets jointly with another BTS group, the Chapter of Surgeons.

Other sub-committees include the Research Committee, the Clinical Trials Steering Group, the Carrel Club (a forum for trainee surgeons) the Nurses Chapter (a forum for nurses, who form a significant membership group) and the Nominations Committee, which nominates consultant members for clinical excellence awards. In view of the increasing clinical importance of live donor transplantation, there is now also an annual Living Donor Forum.

In connection with the Annual Congress, the Congress Organising Committee arranges the Annual Congress and may include both Council and local organising members and provides the abstract and award committees associated with the Congress programmes.

The Council Executive also sits in committee to award research fellowships, travelling fellowships and bursaries. The fellowships are of considerable value. Their main purpose is to fulfil the Society's aim of advancing the study of transplantation, but they also encourage active membership of the BTS. The Roy Calne Award, first made in 1995 (before which it was the Young Investigator's Award), honours Sir Roy's contributions to the science and surgery of transplantation. It is presented for outstanding publications in recognised academic journals. Many of these awards would have been impossible without the financial support (since 1982) of Corporate Members and the attainment (in 1988) of charitable status.

The history of transplantation since the inauguration of the BTS in 1971 is too extensive and involves too many fields of specialist expertise to be adequately summarised here. The following are some of the developments of most interest to the BTS as judged by papers presented at Congresses. In kidney transplantation, led by regimes such as those of McGeown and Morris. Tissue typing was expanded: Ting and Morris applied HLA-DR matching to clinical transplantation in 1978. Following the work of Opelz, the beneficial, and possibly tolerance-inducing, effects of blood transfusion were recognised. The problems of organ donation, retrieval and sharing also received attention and there was increasing awareness of the pitfalls inherent in the public perception of brain stem death and beating-heart donation, which came to a head, in 1980, after the notorious and ill-judged 'Panorama' presentation - 'Are the Donors Really Dead'?

Cyclosporin was first introduced by Calne in 1978 after its potential had been revealed by Borel in 1976. In the 1980s, many contributions charted its role in improving renal transplant outcomes and reducing steroid toxicity. Heart transplantation also benefited significantly. Having abandoned the operation in the 1970s, Shumway in the USA, and others, after making technical improvements, began to achieve results comparable to those for kidneys, in spite of cyclosporin's alarming nephrotoxicity. Monoclonal antibodies also began to be widely used. Improvements in the assessment of patients with liver disease, lead in the UK by Sheila Sherlock, Roger Williams and Elwyn Elias, combined with better donor and organ care, saw a renaissance in liver transplantation, headed by Calne and others. There are now seven UK centres (plus one in the Irish Republic) which have contributed to the world-wide development of the discipline. As results improved among adults, attention focused on techniques to treat children with chronic liver disease. Split liver techniques (in vivo or ex vivo) were a vital advance, allowing the salvation of

many children. The first living donor liver transplant was performed in the UK in 1994. Today many cadaveric livers are split to permit preferential access for children, the remaining larger part of the liver remaining suitable for adult implantation. Adult living donation, auxiliary transplantation, non-heart-beating donation and cell transplantation have also been developed as alternatives to the still limited supply of deceased donations.

The first successful lung transplant, by Joel Cooper, in Toronto, in 1983, also resulted from improvements in surgical techniques and the new immunosuppressive agents. Heart-lung transplantation (which often incidentally permitted a 'domino' heart donation of the recipients relatively healthy heart) was at widely used but later declined in favour of single and/or double lung or lobe transplants, which now may be from living donors. Outcomes have greatly improved, but long-term survival rates are not so good as for kidneys, livers or hearts.

Pancreas transplantation (combined with kidney) which had been pioneered by the team from the University of Minnesota from the 1960s but with only modest success, also began to improve in the 1980s and is now an important option for diabetic patients with diabetes, particularly those with advanced nephropathy due to type I diabetes. Although the combined operation remains the most effective, implantation of the pancreas alone, as well as infusion of pancreatic islet cells have both found a role in suitable recipients. Intestinal transplants, previously impracticable, have gradually improved in outcome since the first successful procedure by Deltz in Germany in 1988. A variety of techniques, sometimes also involving multiple transplants, including the liver, have been developed for a variety of problems, including a number of paediatric conditions, with satisfactory results. On the basic science front, the mechanisms of ischaemia and reperfusion injury have been increasingly revealed, along with the limits for deceased donation which they suggest. The role of complement in rejection has been recognised and the discovery of regulatory T cells has rekindled efforts to understand and induce experimental and clinical tolerance. Tolerance has also been studied through the concept of microchimaerism, proposed as the cause of the relative protection induced by successful liver transplantation. Solid-phase and flow cytometry have improved the accuracy of histocompatibility testing, while immunogenetics enable rapid HLA typing at DNA sequence level. Finally, the introduction of stem cell technology to transplantation science has opened another door through which the elusive form of induced tolerance may be glimpsed. This was the dream of the first transplanters. Paradoxically, today's researches, which suggest that tolerance is not a

perfect 'once-for-all' state of the body, but rather an incomplete, imperfect and temporally variable summation of central and peripheral processes, give hope that antirejection regimes may eventually approximate sufficiently closely to it to become equally effective. The success of cyclosporin, and of later agents (such as tacrolimus, mycophenolate, rapamycin and chimaeric monoclonal antibodies) allowed organ transplantation to become, at last, an accepted procedure, available in thousands of centres throughout the world. As the millennium approached, it became clear that the balance of benefit against risk, in kidney transplantation, was swinging in favour of unrelated live donation, whose results, reversing the predictions of the previous decade, now significantly bettered those from cadaver donors and equaled some forms of related donation. But, as success rates increased, so did the desirability of organs, which some continued to see, not as a 'gift of life', but as an opening for the operation of acceptable market forces. Although most countries, including the United Kingdom, have transplant laws banning commercial donation, illegal marketing persists. While the evils of 'organ trafficking' have been widely exposed, there is some support for the concept of regulated compensated donation.

The BTS in the 21st Century

By the year 2000, the BTS was in a healthy state, with a growing, varied and active membership, which could point both to increasing clinical success and to significant scientific achievement, although some disciplines (eg cardiac transplantation) were less represented than might have been wished. Nevertheless, it still displayed evidence of its informal origin in the early years of transplantation. This had advantages, but could become an embarrassment, even a danger, in the 21st century world. The Society's growth required more administration, as well as a professional secretariat (in earlier years, help from the BSI and hospital staff had sufficed). The diverse interests of more recent membership groups required a voice. Communication, which from 1993 had been made via the BTS newsletter, now relied on electronic contact (the Society's website was professionally reorganised in 2001, by which time the newsletter had ceased publication).

The Annual Congress was getting more ambitious (since 2003 it has used conference centres rather than university facilities) but also more costly. Risk analysis suggested that serious liabilities might fall on the BTS executive and membership in the event of unexpected interferences with BTS activities. Perception of the BTS as 'the Voice of British Transplantation' required a readiness to respond on its behalf, particularly to the media. The disclosures regarding unauthorised tissue retention which lead to the Human Tissue

Act 2004, although not directly involving organ donation, were nevertheless likely to bring it under greater scrutiny. Issues of consent to donation, and to medical treatment in general, were becoming more complex and controversial. Human Rights legislation was another possible source of difficulty. The widening scope of transplantation raised ethical issues, while the continuing shortage of donor organs and the means of overcoming it was an ever-present concern.

Eventually, in 2003, under the presidency of Phil Dyer, the BTS became a charitable company limited by guarantee. The resulting security has been gained at the expense of new statutory duties and enlarged executive powers. The AGM, as well as Council and Executive meetings, must now comply with the Companies Acts. Four Trustees (President, Vice-President, Treasurer and Secretary), while in office, may exercise all the Society's powers, including spending funds on its behalf and making contracts, without requiring Council approval. To avoid gaps in executive experience, the President now serves for two years only, after an 'easing-in' for two years as Vice-President. In 2006, with the approval of the Society, and after a review of 'constituent parts', new arrangements were made for all membership groups to be adequately represented on the Council. The Corporate Members continue their support as Corporate Partners. Most BTS members appeared satisfied with the new arrangements.

To judge by membership alone, the Society is flourishing. There were just under 800 members in 2014, compared to 202 at its foundation, and these figures are stable. The number and variety of abstracts, presentations and posters has increased since incorporation, reaching record numbers in recent years. In the words of Phil Halloran at the Cambridge meeting in 2002, BTS is a 'mother ship' to transplantation and this is borne out by examining the achievements of our members over the decades since 1971, as seen through the lens of BTS meetings, congresses and activities.

The above summary is perforce only a snapshot of the accelerating development of transplantation and its science, omitting many achievements, such as new transplantable parts, improved management of the heart recipient, double lung transplantation, xenografts (still experimental) and emerging pharmacological, immunological and genetically-derived therapies, as well as largely passing over the ethical, legal, logistic, personal, psychological and communal issues still raised by organ donation. This history purports only to tell the story of the BTS, leaving the full tale of transplantation to those

who have created it with their brains, hands, publications and, in the case of donors and recipients, bravery, endurance and trust. What can be confidently asserted, however, is that our Society and its members have at all times been pioneers, discoverers, contributors, promoters and debaters at the forefront of this remarkable science and remain so today, as clearly appears from examination of past and present programmes of our own and sister societies, as well as of the world-wide medical and scientific literature. It is in our hands and those of our successors to ensure that it has a future of equal, and increasing, achievement and enlightenment.

James F Douglas - 2015 (updating the version compiled by Professor Mary G McGeown in 2001 and revised in 2007)

Thanks are due to many BTS members, past and present, who have contributed invaluable information regarding the history of transplantation and of the Society. The author is aware that there may be inaccuracies in and omissions from this brief account.

All appropriate comments and suggestions are welcome.