A meeting of the Association of Surgeons of Great Britain and Ireland took place in Edinburgh on 29–31 March 1989. The President of the Association, Professor Sir Patrick Forrest, was in the chair.

The Moynihan Prize was awarded to J. L. R. Forsythe, P. M. Dunnigan, G. Proud, T. W. J. Lennard and R. M. R. Taylor for their paper 'Reducing renal injury during transplantation'.

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Reducing renal injury during transplantation

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Damage sustained by an ischaemic kidney is reduced by cooling the organ. For this reason kidneys are rapidly cooled during the retrieval operation and preserved at low temperature before implantation. When the kidney is removed from cold storage for implantation into the recipient it gradually rewarms (second warm ischaemic time) and a prolonged second warm ischaemic time has been shown to be a cause of acute tubular necrosis following transplantation. The temperature rise in a kidney during implantation has been poorly investigated and little work to minimize that rise has been carried out. This study investigates, in an animal model, the changes that occur in the core temperature of kidneys during the second warm ischaemic time. A jacket has been designed which greatly reduces the rate of kidney rewarming during simulated operative conditions. Kidneys unprotected by the test system showed a rapid rise in temperature from a mean of 1°C to a mean of 20°C after 45 min, compared with those kidneys placed in the protective jacket in which the temperature rose to a mean of only 8°C in the same time. The jacket is not bulky and is simple to use. Maintaining a low kidney core temperature during the second warm ischaemic time will reduce injury to the kidney and should be part of routine clinical practice.

Keywords: Renal transplantation

Cadaveric kidneys sustain damage during retrieval from the donor, during storage, and during implantation into the recipient. However, such damage may be reduced by lowering the temperature of the kidney during each of these events[1]. Renal oxygen consumption falls exponentially with temperature and this is associated with a 1·5–2-fold decrease in enzyme activity for every 10°C drop in temperature[2]. The three major phases of transplantation when renal injury may occur are:

1. *Retrieval:* kidneys are cooled rapidly in the cadaver donor during the retrieval process using a technique known as '*in situ* perfusion'. The aorta is cannulated and cold flushing of the kidneys performed immediately circulation ceases in the donor. This reduces the ischaemic damage during this period, termed the first warm ischaemic time
2. *Preservation:* the second phase is that of preservation during which time the recipient is selected and preparation made for the transplantation operation. It was shown in the 1960s that kidneys could be safely preserved by ice cooling or continuous hypothermic perfusion[3,4]. Both of these systems rely on maintaining the kidney at a low temperature and therefore this phase is called the cold ischaemic time
3. *Implantation:* the final phase of the transplantation procedure is when the kidney is removed from storage and implanted into the recipient. During the time taken to anastomose the renal vein and artery to the recipient vessels the kidney gradually warms and yet is still without a blood supply. This time interval is termed the second warm ischaemic time

The net result of the ischaemic damage which occurs during these three phases may produce acute tubular necrosis in the donor kidney, causing delay in the onset of renal function. Any delayed function has important implications for the transplant recipient who will need dialysis, who will require to stay in hospital longer and in whom the diagnosis of rejection will be more difficult. There is evidence that delay in the onset of graft function adversely affects long term graft survival[5,6]. When cyclosporin A is used that evidence is particularly strong, with one study showing 75 per cent graft survival at 1 year when the onset of graft function is delayed, compared with 91 per cent when immediate function occurs[7]. Recent reports examining the causes of delayed graft function have shown that a long second warm ischaemic time leads to a significantly increased risk of delayed function[8,9]. As it is known that warm ischaemia will severely damage a kidney in 60 min[10] and that

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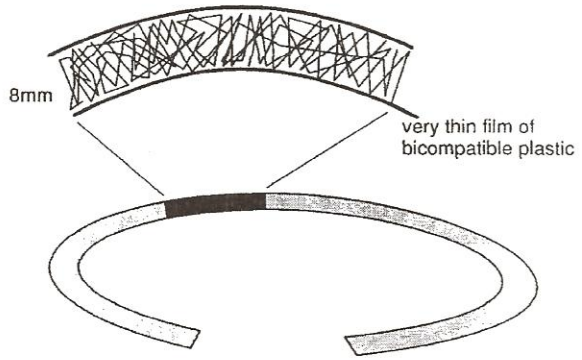

Figure 1 *Illustration of present design jacket*

kidneys can be stored for up to 72 h when cold, there are obvious advantages in preventing rewarming of the kidney before it is connected to the circulation of the recipient. Until now only basic attempts have been made to keep the kidney cool during the transplant operation, usually by wrapping it in gauze soaked with cold saline.

The aims of the study were to investigate the temperature changes that occur in the kidney during the vascular anastomosis phase of the transplant operation in an animal model, and to design a system that would keep the temperature of the cooled kidney below 10°C for 40 min. A realistic system would need to be simple to use, non-bulky, allow easy access to the renal vessels for anastomosis and be either disposable or easy to sterilize.

Materials and methods

An animal model was designed to reproduce the operative conditions that exist during the second warm ischaemic time of the transplant operation. Pig kidneys from the abattoir were used. The pigs were killed by stunning and exsanguination and their kidneys were removed within 20 min of death and cooled. Two methods of initial cooling were used. The kidneys were either infused via the renal artery with cold perfusate solution and then placed in ice, or placed in ice without prior infusion. The core temperature of the kidneys on removal from cold storage was the same regardless of which cooling method was used and comparisons were always made between paired kidneys which were cooled in the same way. All kidneys were placed in plastic bags and stored in crushed ice in the same way as human kidneys are preserved in the UK.

The two kidneys were removed from cold storage in an operating theatre. One kidney was wrapped in gauze soaked in ice-cold saline. The second kidney was placed in the system under test. If there was a size discrepancy between the two kidneys, the larger one was used as the 'test' kidney. Thereafter, the kidneys were subjected to exactly the same conditions. The energy striking the experimental surface was controlled as follows. First, the kidneys were supported on a thin film of plastic over a water bath, the temperature of which was maintained at 30°C. Secondly, energy from the operating theatre light was measured using a lux meter and maintained at 30 klx by adjusting the height and focus of the light. This figure represents a power dissipation of 142·5 mW/cm^2.

Temperature was measured using a minithermocouple probe attached to a digital meter data logger (Grant Instruments, Cambridge, UK). This enabled accurate temperature measurement to be made every minute for the first 5 min after removal from cold storage. Readings were then taken every 5 min up to 45 min. This time was chosen as it represents the upper limit of the second warm ischaemic time in clinical renal transplantation on our unit. Temperature measurements were recorded at four sites: (1) water bath, (2) air temperature at experimental surface, (3) core of kidney (control), and (4) core of kidney (test).

Cooling systems tested

Several systems were tested and discarded for a variety of reasons: continuous flow of cold saline or gas around the kidney (these methods were cumbersome and difficult to use); an envelope of ice around the kidney (this was bulky and difficult to handle); aluminium foil (this was much more pliable and moulded to the desired shape well, however, it did not perform well in laboratory bench tests because of accelerated heating in certain circumstances).

Consideration of the basic physics of the problem suggested that the thermal conductivity of the material in use was the major factor which could be altered without increasing the bulk of the 'jacket'. An easily available substance with a low thermal conductivity is air. It was from this simple idea that the prototype was developed and improved to become the system tested (*Figure 1*). It consists of two thin films of a biocompatible plastic, which sandwich a weave of a similar plastic containing air trapped among the fibres of the weave. The jacket thus formed measures 8–10 mm in thickness and can be used for small or large kidneys. It is closed around the hilum of the kidney by a simple draw cord which allows the renal vessels to protrude.

Results

Throughout all experiments, the water bath temperature was maintained in the range 27–33°C and the air temperature in the operative field was recorded as 28–38°C. Mean results over 12 paired experiments for these two parameters are listed in *Table 1*. On removal from the preservation system, the core temperature of all kidneys ($n = 24$) was 0–1°C (mean 0·6°C). In 12 paired experiments, the kidneys that were allowed to warm sustained a predictable rise in temperature of 2°C (mean 1·9°C) per 5 min interval, from 5–45 min. The core temperature of these kidneys was always above 10°C by 20 min. The final temperature at 45 min was 16–25°C (mean 19·6°C). The core temperature of the paired kidneys placed in a cooling jacket rose at a mean of 0·9°C per 5 min interval in the 5–45 min period. The mean temperature at 45 min was 8·0°C and was always below 10°C at this time. These figures are listed in *Table 1* and illustrated in *Figure 2*.

Table 1 *Mean temperatures recorded in 12 paired animal model experiments*

	Temperature (°C)			
Time (min)	Water	Air	Core kidney (normal)	Core kidney (test)
0	32·2	31·0	0·6	0·6
1	32·0	31·1	1·1	0·7
2	31·4	31·2	1·7	0·8
3	31·0	30·8	2·4	0·9
4	30·6	30·0	3·1	1·1
5	30·9	30·4	4·0	1·3
10	30·7	30·5	6·3	1·8
15	30·1	30·4	8·8	2·5
20	30·2	30·2	11·5	3·4
25	30·0	29·9	13·4	4·2
30	29·8	29·6	15·2	5·1
35	29·2	29·5	16·7	6·1
40	29·6	29·4	18·1	7·2
45	29·9	29·5	19·6	8·0

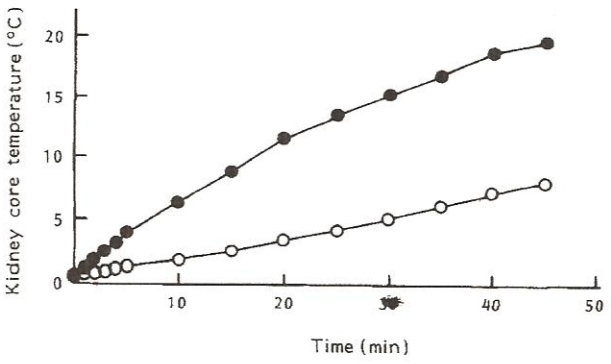

Figure 2 *Mean temperature recorded in 12 paired animal model experiments: ●, control kidney; ○, kidney with jacket*

Discussion

This study has demonstrated that the core temperature of kidneys stored before transplantation is between 0 and 1°C, a fact not always appreciated by transplant surgeons. It is important to place the kidney in fluid during ice preservation as failure to do so may allow freezing of the parenchymal tissue with resulting intracellular crystal formation and cell damage. Indeed, recent evidence suggests that such low temperatures may not be ideal for kidney preservation[11].

A number of studies have demonstrated that keeping a kidney cool during a period of ischaemia improves ultimate function[12,13]. It is the practice of some surgeons to pour aliquots of cold saline intermittently on to the kidney during the second warm ischaemic time. Nevertheless, in a separate experiment this was shown not to lower the core temperature and it had minimal effect on slowing the rate of temperature rise. To obtain a satisfactory cooling effect, cold saline had to be run over the kidney in a continuous stream.

Other methods of keeping the kidney cool[14] (using jackets) during the second warm ischaemic time have not met with acceptance owing to the bulk or complexity of such devices, which make the performance of the vascular anastomoses more difficult. The cooling system employed must not only keep the kidney cool but also must not handicap the surgeon. A jacket, such as the one described, is non-bulky, simple to use, disposable, and allows access to renal vasculature while still maintaining the kidney at a low temperature. This jacket is being commercially developed and when a suitable sterile form has been made it will be tested during clinical transplantation.

In the early days of transplantation it was recognized that ischaemic injury must be minimized. This objective has been largely achieved during the retrieval operation and during a limited preservation period. Slowing the rate of the temperature rise during the second warm ischaemic time will further reduce ischaemic injury and should, therefore, become part of clinical practice.

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