Organ Procurement

Chairman: G P J ALEXANDRE, Louvain, Belgium

G P J ALEXANDRE: I would like to introduce you to the members of the panel:

Professor J L Terpstra of the Netherlands
Doctor A Pillen of Belgium
Professor Claes of Sweden
Doctor Jakobsen of Norway
Professor Kreis of France

We all know that transplantation has made progress over the past years. Transplantation can be a cure for many of our patients, but unfortunately we do not have enough kidneys to transplant, and in particular there are not enough cadaver kidneys. In this discussion we shall try to find the reasons why we have an insufficient number of kidneys and secondly, what guide lines we should use to increase the numbers.

The plan of the discussion is as follows: first we will speak for a few minutes about the use of living donors. Should we continue to use them and in what circumstances? Then we will talk for 25 minutes about ways of obtaining more cadaver kidneys. Dr Pillen will talk for a few minutes about the criteria of death before removal of cadaver kidneys. The next point will be how best to prepare cadaver donors: what techniques should be used for the removal of the kidneys and how best to preserve them, and finally how to choose the best recipients.

Professor Kreis, would you like to talk about the selection of live donors, should we still use them and in what circumstances?

H KREIS: Our opinion at the Necker Hospital in Paris is that living donors should only be used when there is an HL-A identical sibling, because our past experiences has lead us to believe that the results of living donor transplantation from non-identical individuals are no better than transplantation with compatible cadaver kidneys.
ALEXANDRE: Is there another member of the panel who wants to comment on that point?

A JAKOBSEN: The opinion in Oslo is that we must continue to use living donors in cases where it is possible. There are two reasons for this: firstly because there is a shortage of cadaver kidneys which I think will continue, and secondly, if one is to get anywhere with immunological 'engineering' like enhancement and inducement of tolerance, these experiments will have to be carried out with living donors. I believe it to be impossible to tackle problems like enhancement in cadaver kidney transplantation with present techniques. This is one very important reason why one should go on using living donors.

ALEXANDRE: Is there any member of the audience who would like to speak on this point?

van BREDA VRIESMANN (Leiden): Professor Kreis, you state that you transplant only HL-A identical living related kidneys: would you care to comment on HL-A identical MLC different, and MLC identical but HL-A different kidneys? For example, do you transplant an HL-A identical but MLC different sibling?

KREIS: Well, sometimes in special cases we do accept HL-A identicals for transplantation with an unfavourable MLC, but not always.

van BREDA VRIESMANN: I should like to raise the question of living donors for children. Would it not be right to transplant a child as quickly as possible and therefore would you not make an exception and accept a parent donor?

KRIES: We are not transplanting many children at the Necker Hospital. If the child is doing well on dialysis we wait for a cadaver kidney. However, if he is not doing well we will accept a kidney from one of the parents.

ALEXANDRE: Now we turn to the problems of cadaver kidneys. What are the reasons why only a small percentage of the potential cadaver donors are utilised? Is it due to medical opinion, public opinion or both. It would seem to me to be due to both. We have to find ways to increase the procurement of cadaver kidneys. Dr Jakobsen will speak about what measures could be taken, because in Norway they have developed an unique organization for the collection of cadaver kidneys.

JAKOBSEN: Norway is, geographically, an elongated country with a very scattered population of only 3.7 million. Figure 1 shows a map of Norway
with about 20 dots indicating places undertaking the care of uraemic patients with hospital dialysis facilities. Some of these centres have 10 to 15 patients, whilst others only have one or two patients on dialysis. These patients are always managed by the local nephrologist or physician, with whom the members of the transplant team in Oslo have frequent and regular liaison. We meet them two or three times per year when we discuss practical methods and try to work out a common policy. The nephrologist also coordinates with the local neurologist and radiologist, and the local surgical team. We have, in Norway, brain death criteria which allow us to preplan the donor nephrectomy. We also need the help of the neurologist, the radiologist for carotid angiograms, and the surgical department. We made it clear from the beginning that people from the transplant team in Oslo would go out at any time of the day or night to assist. For example, we once took an operating theatre
nurse, and a radiologist. Last Monday we went 400 km to bring kidneys for perfusion as the local perfuser had left to attend a Congress in Vienna!

There is a group of hospitals around Oslo within 100-150km, which can be reached by car, but for distant hospitals we use small charter 'planes and can reach most places within an hour and a half. Our criteria for donor nephrectomy and the investigations for brain death allow us time to make travel arrangements. Table I shows what we have been achieving by this

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<th>Oslo hospitals</th>
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<td>1971</td>
<td>40</td>
<td>8 (16%)</td>
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<td>1972</td>
<td>28</td>
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<td>1973</td>
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method. In 1972 and 1973 almost 50% of our cadaver kidneys came from Non-Transplant Centre hospitals. This is just the beginning and we hope to increase it. We are also hoping that the local teams will become more experienced and manage without needing us to fly out as we often do at the moment.

ALEXANDRE: Thank you Dr Jakobsen. May I ask Professor Claes what is the organisation in Sweden?

G CLAES: We have the same organisation as in Norway, which we started in 1961. However, in Sweden it is not possible to remove kidneys from brain dead patients. We have to wait for cardiac arrest, so it is impossible for the transplant team to go to distant hospitals. For that reason we arrange to teach local surgeons how to remove the kidneys. We have compared the results of kidneys removed at the transplantation centre in Gothenborg with those removed from distant hospitals, and the results are exactly the same. Obviously, the local surgeons can remove kidneys just as well as the specialists at the Transplantation Centre! At the moment, 33% of all kidneys are removed by distant hospitals accounting for 50 kidneys per year.

ALEXANDRE: May I ask you a question. When the kidney is removed by the local team, is this the general surgical team? How many times did you go there to teach them and were any of them trained in Gothenborg?

CLAES: We used to go out just once to teach them how to remove the kidneys; however the kidneys are not removed by the younger surgeons but by the senior surgeons.
JAKOBSEN: I might just add that what we have been doing in Norway was very similar to what we learnt in Gothenborg. Our initial plan was to go out once, remove the kidneys ourselves and show them how to perfuse them, explaining all the snags involved in removal and perfusion. On the next occasion we acted as assistants, allowing the local surgeon to remove the kidneys and another person, for example the nephrologist, to take care of the perfusion. The third time we allowed them to do it themselves.

CLAES: I think it is very important to report back the result of a transplantation. We telephone two to three days later and again when the patient is leaving hospital, giving the fate of the organ they collected.

ALEXANDRE: Is this the way you reward the local teams who give you the kidneys, or do you have some other ways to recompense them for their work?

CLAES: Recently there has been a recommendation from the Government to the local hospitals that they should participate in the removal of kidneys for transplantation, but there is no financial inducement.

ALEXANDRE: I think that Dr Terpstra has something to add.

J L TERPSTRA (Leiden): We in Leiden, Holland, do the same as Dr Jakobsen described, more or less being a 'flying squad' travelling round the country removing kidneys. We also try to stimulate local and distant hospitals by visiting them and getting our neurologist, nephrologist, surgeons and Mr Schippers from Eurotransplant to talk to them. In fact the results are not very impressive.

We now use journals and advertisements more aggressively than we would have dared four or five years ago in order to make the public more aware of the need for kidneys. It is our experience that there are some hospitals which always collect cadaver kidneys because they are really interested in transplantation or dialysis. Many hospitals who have donors fail to think about it at the time, but remember a week afterwards.

ALEXANDRE: I think that part of the difficulty in getting kidneys is that the donors are generally treated in Intensive Care Centres, which are not involved in the treatment of the recipients. It is our experience that most frequently these Centres never think of the possibility of providing donor kidneys. Another factor is the 'comportement' in the Intensive Care Centres. For the Intensive Care staff the death of a patient is a failure of their treatment. They dislike failing and they resent the appearance of a transplant team at this time. I therefore feel it is important that we should find a way to spare
their feelings and reward them for the work they are doing. In hospitals where there is a permanent transplant team the problem is smaller because the doctors and nurses of both the transplant and Intensive Care teams are either connected or, at least, acquainted with each other. It is much more difficult for the Intensive Care Centres of hospitals without a transplantation team. I really think we have to reward them for this work, especially as on most occasions it is late at night, during the weekend or holidays. In recent months we have discussed ways of rewarding them with Eurotransplant in Leiden. I wonder if Mr Schippers from the Eurotransplant in Leiden would give us his thoughts on this problem?

MR SCHIPPERS (Eurotransplant, Leiden): I would like to refer back to what Dr Claes said. I believe that the motivation of people in the donor centres is primarily the responsibility of the dialysis doctors. It is they or the internists who are most interested in transplantation, and who should motivate the local teams. Another point to consider is that in many countries the State is paying for the medical care. This is not the case in Holland, Belgium and Germany, where doctors have private incomes and private patients and insurance companies pay for their services according to mutual agreements. We have a strong feeling that the financial aspects of taking kidneys might be important. We therefore propose to pay a certain amount of money to the hospital administrations. This amount of money is calculated on the number of procedures which, on average, are done at cadaver nephrectomy. The hospital administration should then reimburse the individual specialist. The cost of this system, which will be organised centrally will be charged to the recipients. Since a number of kidneys are removed but not used, it has to be done centrally: insurance companies will not pay unless the kidney is used. However, the cost to the recipient will include the cost of the unused kidneys.

ALEXANDRE: Thank you Mr Schippers. I think that Professor Kreis would like to add something.

KREIS: I think there are other ways to reward the team who care for the donors. If they are not calling us more often it is not because they are not paid, but because there are not enough beds to treat the patients. I think that a way to increase the number of donors reported to us would be to ask the Government to increase the number of beds in the Intensive Care Units. That is what we are trying to do in France now.

ALEXANDRE: I would like to ask Dr Claes if the paper sent out by the Government to all Intensive Care centres regarding kidney donors was followed by any increase in the number of cadaver donors reported?
CLAES: I do not know yet, because this recommendation was sent out only a few weeks ago. Our last experience of this kind was favourable: when we had a publication in the Swedish Medical Journal on this subject it increased the amount of kidneys removed by other hospitals.

P GARRELL (US Army, Europe): I am very interested to hear these comments. Is it difficult to get permission to donate kidneys: do you have to get permission from the family? I think a bigger problem is to educate the public. We are concentrating too much on nephrologists and urologists. In the USA, for example, a patient with a head injury is brought into a suburban hospital without a large Intensive Care Unit, without a nephrology/urology service and where the doctor knows little about transplantation. The shock to the family, who knew a healthy person a few minutes ago, is tremendous. It is harder to get permission for a kidney transplant than it is for an autopsy. I find that more help comes from newspaper articles and television programmes which deal with the social aspects of transplantation. People then go to their local doctors. A lot of difficulties have resulted from sending strange doctors by helicopter to hospitals around the Cleveland area. You need the family doctor to get permission to remove the kidneys.

ALEXANDRE: That is only when you need the permission of the family, which I believe is the law in the United States. There are some countries where it is not necessary to have permission: for example the new law which is eventually to be evolved in Italy will not require the doctors to obtain permission from the family. My own opinion, for various reasons, is that we should not have to ask the family’s permission. One fundamental point is that when you are alive you are obliged by law to help other people, and I think it is a basic contradiction that you are obliged to ask permission to do this from the family of a dead patient. Also, the moment when a member of the family has just died is not the time to ask permission from the family.

I would now like to ask Dr Pillen what criteria of death he would like to see as law and what are the feelings about the present criteria of death in 1973?

A PILLEN: First, cerebral death is to be considered as conventional death: this is very important. Second, the time of evolution of irreversible brain damage is not so important. In our opinion the most important thing is the clinical context, and there must be structural brain damage and a hopeless situation after all possible treatment.

We can use technical investigations of which the EEG is of great value. The timing of the EEG — 48 or 34 hours as suggested by the Harvard Committee and Memorial Hospital is not crucial. What is important is the clinical
context where you know that the patient has irreversible brain damage with no possible hope of recovery. In this situation artificial respiration can be stopped regardless of whether the kidneys are used for transplantation.

ALEXANDRE: I would like to hear more on the zero EEG. For instance, I would like to know the minimum time you advocate for a zero EEG before you switch off, because this is most important in some countries. In Italy, for example, they want a zero EEG for 24 hours, whilst in other countries—for example France, I think it is 12 hours.

A PILLEN: Usually, I think that a cerebrally dead person has the right to have a 20 minute EEG, as in a normal patient. One documented EEG of 20 minutes is in my opinion, enough. It should not be repeated in all cases. I will give you an example of where in my opinion, you could remove kidneys from a patient with a quite normal EEG. It may surprise you but in some cases of traumatic head injuries where one cerebral hemisphere is lying on the shoulder of the patient, and you take an EEG of this cerebral hemisphere, lying outside the skull, you may observe electrical activity with quite a normal EEG. Would you treat such a patient?

In summary, within a given clinical context one 20 minute EEG at maximum amplification is sufficient, especially when we know the aetiology is structural hemispheric damage.

KREIS: I entirely agree with Dr Pillen. The clinical context is much more important than the EEG. In France we are obliged by law to wait for a 'flat' or zero EEG, but we do not have to record the time of the EEG.

PILLEN: In Belgium we have tried to get a law that does not even mention the EEG, where we just have a text saying that three doctors have to make a diagnosis of death.

Van der WERF (Miami): It is the opinion of our Donor Committee that it is very important to differentiate between structural brain damage and so-called anoxia. If anoxia is present you must evaluate the donor more carefully and probably take 24 hours to do so. But if there is severe structural brain damage, which is not compatible with life, you can more or less declare cerebral death on the spot. It is a new trend in our Committee and I would support it because it is very important to be clear about the situation.

PILLEN: I think that when anoxia is secondary, for example, to cardiac arrest during operation, the clinical situation is entirely different. You should give this patient the chance of recovery. In these circumstances you do not find a zero EEG at the beginning, but a typical EEG pattern with repetitive paroxysms. In secondary anoxic brain damage when the paroxysms
disappear and you have a zero EEG, then the patient is lost, but the spontaneous evolution to conventional death can be much longer than in traumatic cases where there is brain oedema. Fifty per cent of cases with closed head trauma die conventionally within 48 hours. With anoxic secondary brain damage they may survive a week with a zero EEG before they finally die.

van BREDA VRIESMANN: I just want to make a comment, not to ask questions. I think that we are using very dangerous language. The moment you even talk or mention the fact that the clinician is going to determine whether someone is dead or not, you are in dangerous waters. I think that every lawyer would accept a flat EEG as a final answer. If you go above and beyond that, I think you will have a great deal of trouble outside the medical profession.

PILLEN: When we do an EEG, it is because it is an objective document, since there could be a question of law involved, but I believe that as a trained clinician and neurologist you do not need to have an EEG to say someone is irreversibly lost.

JAKOBSSEN: A transplant law in Norway which is not as yet operative states nothing about the criteria of death. The diagnostic criteria that are being used are that a cerebral angiogram is performed with bilateral selectives of the carotids and at least one vertebral artery.

PILLEN: In my opinion it is very difficult to carry out this performance in every patient because some people may have cerebral death with normal cerebral circulation. What do you do with these patients?

JAKOBSSEN: They are not accepted as donors.

PILLEN: What does the law in Norway say about the permission of the family?

JAKOBSSEN: The law states that there is a presumed wish to donate organs. We have to try to get in contact with the family and ask their permission, but this is not a definite requirement. When we cannot contact the family, and this often happens in our elongated country, we can remove organs without telling the family until afterwards.

ALEXANDRE: We now have to go on to the discussion of what happens when it has been decided to remove the kidneys. The question arising is how best to prepare the donor, and is pre treatment of the donor any help. By pre treatment I mean the treatment of the donor with cortisone, endoxan, or some other drugs before the removal of the kidneys. I would like to ask Dr Jakobsen to comment.
JAKOBSEN: We have, as I indicated, removed kidneys from patients with a beating heart, and investigated their function. We discovered that something like 25% did not have an immediate diuresis. After communicating with Loekkegaard in Denmark, we started using chlorpromazine as a pre-treatment. Of 63 cadaver kidneys removed without pre-treatment there was immediate function in 46 (73%), with a need for post-operative dialysis in 15 cases (23%) (Table II). Hyperacute rejection occurred in 2 kidneys. Since pre-treatment with 250 mg of chlorpromazine in 500 ml of 5% glucose intravenously, given during the last half hour before donor nephrectomy, all 13 kidneys treated this way had immediate function. Since we made this observation we have removed a further 66 kidneys and to the best of my knowledge all 66 have had immediate function with no need for post-operative dialysis.

ALEXANDRE: I wonder if there is in the room some member of the staff of Dr Guttmann, Canada, or someone who is well acquainted with his work, because I know that he is pre-treating the donor with 5 mg of methyl-prednisolone, cyclophosphamide and medroxyprogesterone. He claims that they have a one-year graft survival of more than 90% with this form of pre-treatment, possibly because the passenger leucocytes in the graft are killed.

KREIS: I have no experience with this kind of pre-treatment, but I spoke with Dr Guttmann and I saw the results. One of the objectives of the preparation of the donor has as its goal the destruction of passenger leucocytes. He proposes that 6 hours before nephrectomy, the donor should be injected with 5 gm of Soludrone and 3 gm of cyclophosphamide. He took two groups of transplanted patients, 12 patients without pre-treated cadaver kidneys and 9 patients with pre-treated kidneys. He concluded that the immunogenicity of pre-treated kidneys is reduced.

But several objections can be made. One is the necessity for a 6 hour delay which prolongs the waiting period before the kidneys can be removed. Second, the circulating lymphocytes of the blood and possibly those of the lymph nodes are destroyed or altered by this pre-treatment. All organs to be used for HL-A typing and especially for cross-matching must therefore be removed beforehand. Finally, Guttmann's series is small and many other
factors may have effect on the results. In conclusion we might say that
haemodynamic preparation of the donor is indispensable and that whenever
possible pre treatment with phenoxybenzamine and/or chlorpromazine should
be used. Immunological pre treatment is an interesting area for further re-
search.

ALEXANDRE: Thank you very much. Is there anyone else who wishes to add
something to this pre treatment problem?

van BREDA VRIESMANN: As far as I know Guttmann needs a very long time
before the nephrectomy for his regimen to be effective. Now as I understand
it, if he injects the prednisone and cyclophosphamide four hours before death
it does not work at all; it has got to be between 8 and 12 hours. Is that not
so?

KREIS: He told me 6 hours were enough.

van BREDA VRIESMANN: In donor pre treatment what is the histology of the
kidneys after transplantation? If you assume that you are killing donor lym-
phocytes there may be less MLC reaction in the graft, or attenuation of graft
immunogenicity. To my knowledge Guttmann does not know which one of the
two it is. Is this correct?

KREIS: That is correct.

van BREDA VRIESMANN: Is the increase in survival of the pre treated grafts
also related to tissue typing?

KREIS: Tissue typing was done for donor selection, but the data have not
been analysed further.

ALEXANDRE: Now we must go on to the problem of removal of the kidneys
and the techniques of removal. I think there is much to be said about tech-
niques, as many kidneys are not removed as well as they could be. I would
like to ask Dr Terpstra to talk about that.

J L TERPSTRA: From what we have heard, I now take it for granted that
there is a donor in a good condition with kidneys to be removed! The idea is
to do the least possible harm to the kidneys. I think two things are very im-
portant: first that one has up-to-date knowledge of preservation; second, that
you know your surgical anatomy very well. I will not go into the minute de-
tails of nephrectomy. You can find that in the Eurotransplant Manual. One
thing of great importance is that you use a very wide exposure to take out the kidneys. The situation is made easier when you only have one artery on each side: then they can be easily cannulated, tied off and put on the perfusing machine. The problem arises when you have multiple arteries or early branching of the renal arteries. Personally I think it is mandatory that before you start dissecting the kidney you should free the distal aorta, from the renal veins down to the bifurcation, and inspect the aorta for multiple arteries. If there are multiple arteries it is advisable to take out the aorta and kidneys en bloc with enough aorta above and below the renal arteries to tie off when using a perfusion machine or introducing a cannula. In this way you can prevent lesions to the renal arteries. The en bloc removal prevents internal damage to small arteries by cannulae or ligatures. In the case of multiple veins, it is said that of a pair of veins of equal size, one can be tied off; I think you can tie a small vein without worrying, but Belzer told me that in one of his cases with two equal veins there was venous engorgement of half of the kidney afterwards and the kidney had to be removed, so it is important to take a venacaval patch too in such cases.

There is an easier manoeuvre for getting good access, particularly for en bloc resection of aorta and kidneys: when you open up the retroperitoneum, cut the peritoneum around the caecum, go up laterally along the ascending colon up to the venacava and then place all the gut on the chest of the donor. What is left is the descending colon; you then cut the mesocolon, tying off the inferior mesenteric artery. This gives you ample access to the kidneys and a good view. I think haste is to be avoided. We have done 80 or 90 donor nephrectomies in the last seven years and it still takes one hour for the whole procedure. Regarding preservation, when you use phenoxybenzamine you should be aware that it has to be in the body for 25 to 30 minutes before good vasodilatation is achieved. We always use heparin before starting the operation. Years ago we advocated the introduction of a cannula into the common iliac artery and perfusion with iced saline solution containing procaine and heparin at 4°C under pressure. Four or five litres were flushed through the aorta while the left common iliac artery and the aorta above the diaphragm were clamped off. This produced an isolated perfusion of the abdomen. It worked very well in combination with an 8 to 10 hour preservation, using the method of Gelin and Brunius, but when used with the Belzer technique with his machine and plasma it does not work at all. So now, in beating-heart donors, we free the kidneys first and start cooling directly via the renal arteries using Collins’ solution. In donors with poor or no circulation we start cooling via the common iliac artery, using 1 litre of Dextran 40.

In Eurotransplant we have data on the percentage of kidneys lost because of technical errors. In the 8 months from November 1972 to June 1973, 24 kidneys were lost, either from technical errors or machinery faults. During
the same period 260 transplants were performed. A 10% loss of kidneys which could have been transplanted is something to think about. The conclusion I draw from this is that the best surgeons should do the nephrectomy and the residents should put the kidney into the recipient!

ALEXANDRE: Well, I think it is better to have two good surgeons to do both! I would also like to say that for more than a year now we have been using a very long incision, starting at the pubis and extending up into the sternum. It takes only a few minutes to open up the sternum and it is very easy. Since we have done this we get such a good access to all the arteries and veins that it becomes quite an easy job even for a resident.

I would like Dr Kreis to give us his views of preservation methods now being used by France transplant.

KREIS: Renal transplantation is regarded today as the main form of treatment for end stage renal failure. For that purpose it is necessary to use cadavers as the major source of kidneys.

European data at least, lead to the belief that a good match between donor and recipient is one of the requirements for improved transplantation results. A large pool of recipients is consequently needed; therefore long distance transport of kidneys becomes mandatory to achieve the use of all available kidneys. Sharing is already necessary, even if one does not believe in the efficacy of HL-A matching. It therefore follows that we must preserve a kidney for many hours. From our past experience, we can assume that a 24 to 30-hour delay has always been sufficient to perform transplantation adequately. Beyond that, a real benefit would only be obtained with storage periods as long as 6 to 7 days. In these conditions, it would then be possible to perform different selection tests, for example the MLC test.

Taking organ conservation another step further would lead us to the concept of indefinite preservation time and 'organ bank'.

Every time we argue for one preservation method against another it is essential to define our eventual goal. For example, there would be no point in discussing the value of simple surface cooling for long term kidney preservation and on the other hand freezing would be a nonsense for a few hours' storage only.

Now, the question raised is to know whether permanent perfusion machines are more efficient than surface cooling. I will try to answer that question taking into account (1) the selection of the best recipient based on HL-A criteria; (2) the use of all available kidneys, and (3) the organisation of renal transplantation as a daytime routine, and not as an emergency.

A great variety of machines are now available on the market, any differences being mainly in their design. Their efficiency in kidney preservation is no longer in question. A lot of valuable experimental work has shown that
storage can be regularly obtained for 2 or 3 days. It is beyond doubt that the perfusion solution plays a more prominent part than the machine itself.

In human renal transplantation the mean preservation time reported in the literature is usually low: less than 24 hours. This is due to the fact that longer periods of storage are generally not necessary. However, it has been said that the perfusion characteristics of the kidney give some prediction of the post-operative function, especially when the kidneys undergo prolonged warm ischaemia and when terminal hypotension of the donor exists.

Such cases are associated with a high rate of failure and delayed function. Perfusion characteristics should therefore be of considerable clinical value in the transplantation of these kidneys.

In fact, the significance of a low flow rate is unclear and the relationship with the post-operative function is obscure. We can only say that a non-perfusing kidney on a machine will not be revascularised in the recipient. Moreover, in some cases, a good kidney can be damaged by the machine itself. A recent paper by Terasaki et al. has emphasised the fact that kidneys preserved with perfusion may not do as well as surface cooled kidneys. In spite of their postulated advantages, machines have major inconveniences. Their volume, weight, complexity and cost prevent kidney transport on a large scale. Despite their theoretical advantages we do not think that machines are the practical solution in human cadaver kidney preservation for transplantation. Can simple surface cooling methods compete with permanent perfusion techniques? We think so, especially if kidneys are initially washed through with an electrolyte solution of intracellular composition, as it was first demonstrated by Collins and co-workers. It is possible to preserve such kidneys for 48 hours with nearly a hundred per cent success after autотransplantation and immediate contralateral nephrectomy as shown in Figure 2.

![Creatininaemia after renal autotransplantation. (10 pig kidneys preserved 48 hours - Collins' technique)](image)

Figure 2. Creatininaemia after renal autotransplantation. (10 pig kidneys preserved 48 hours - Collins' technique)
Figure 3. 48 hours cold preservation, 45 minutes warm ischaemia.
(Pig kidneys - Collins' C₇ solution)

Figure 4. 48 hours preservation. (Pig kidneys - Collins' C₂ solution, without magnesium)
More recently, in an experimental series which is still in progress, we have shown with Dr Barbanel that a 3-day preservation can be obtained, provided that phenoxybenzamine is infused intravenously before nephrectomy.

Some investigators have suggested that 24 hour preservation was not possible, using Collins' solution, if the donor first had a period of warm ischaemia. Nevertheless, Lokkegaard and co-workers have been able to preserve pig kidneys for 24 hours after one hour warm ischaemia time.

Figure 3 shows the results obtained in our laboratory using pig kidneys preserved for 48 hours after a 45 minute warm ischaemia time. Two pigs died during the first few days after transplantation. In the remaining four pigs, however, after an initial renal failure period, creatinine returned to normal. The autopsy showed rupture of the kidney in both cases. Two other objections have been raised in relation to this method. One is the risk of magnesium phosphate crystallisation in the Collins' C₃ solution. In fact, this occurred mainly in vitro. To prevent this it is necessary to add the magnesium just before the use of the solution and the kidney must always be stored in a magnesium free solution. In fact this electrolyte does not seem to be of great value.

Figure 4 shows the results obtained in 48 hour pig kidney preservation using Collins' solution without magnesium. They are similar to those obtained with the complete formula. The other objection is based on the absence of flow rate data when kidneys are preserved in this way. We have shown with Dr Barbanel that it is very easy to measure the flow rate of the initial wash-out period and then once again at the end of the preservation period. We have recorded the variation of intrarenal resistance during the storage period in

![Graph](image)

**Figure 5.** Intra-renal resistance before and after cold storage
several preservation experiments and we can say (Figure 5) that there is no increase in the resistance of functioning kidneys and when an increase in the resistance occurred, kidneys did not function. However, a low stable resistance is not a valid criterion for the viability of the kidney.

We have applied this technique in clinical practice since 1969 and the results obtained by four transplantation groups in Paris were reported in 'The Lancet' in October 1972. They demonstrate the same post-transplant outcome, whatever the preservation time was: the range was from less than one to sixteen hours.

At the Necker Hospital, graft ischaemia was increased progressively as we have gained confidence in our preservation technique. In 1972 nearly 50% of kidneys were preserved more than 12 hours. The longest ischaemia time being 23 hours (Figure 6).

Our own results with long ischaemia periods are analysed in Tables III, IV and V. Three groups were defined:

- **Group I**: 0 to 6 hours
- **Group II**: 6 to 12 hours
- **Group III**: 12 to 23 hours

Series A (Table III) included kidneys with less than ten minutes warm ischaemia, while series B corresponded to kidneys with between ten and sixty

![Figure 6. Preservation time (100 human cadaver kidneys)](image)

minutes of warm ischaemia. In Table V it is seen that the incidence of immediate function is slightly better in Group I, but the difference between the groups is not significant.
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<td>6 - 12</td>
<td>554 ± 18</td>
<td>35</td>
<td>17 (48.5%)</td>
</tr>
<tr>
<td>III</td>
<td>&gt;12</td>
<td>935 ± 39</td>
<td>19</td>
<td>10 (52.6%)</td>
</tr>
</tbody>
</table>

*(Series A warm ischaemia <10 minutes)*

**Table IV. Percentage fall of serum creatinine from day 0 to day 3**

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Ischaemia (hr)</th>
<th>Series*</th>
<th>Number of cases</th>
<th>Mean % fall in serum creatinine days 0-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0 - 6</td>
<td>A</td>
<td>21</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>2</td>
<td>45</td>
</tr>
<tr>
<td>II</td>
<td>6 - 12</td>
<td>A</td>
<td>13</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>&gt;12</td>
<td>A</td>
<td>9</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>1</td>
<td>75</td>
</tr>
</tbody>
</table>

* Series A warm ischaemia <10 minutes  
  Series B warm ischaemia 10-60 minutes

**Table V. Kidney transplant function: sixth month (Series A)**

<table>
<thead>
<tr>
<th>Group</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>40</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td>Number of functioning grafts</td>
<td>28 (70%)</td>
<td>22 (66.5%)</td>
<td>7 (63.5%)</td>
</tr>
<tr>
<td>Mean creatinine clearance (ml/min)</td>
<td>83</td>
<td>76</td>
<td>79</td>
</tr>
</tbody>
</table>

Table IV shows that in functioning kidneys the percentage fall of serum creatinine from day 0 to day 3 is the same in the three groups.

Six months later 70% of the kidneys are functioning in Group I and 63.5% in Group III. The difference is not significant. Among the functioning kidneys, the mean creatinine clearance is 83% in Group I and 79% in Group III (Table V).
CONCLUSION

So far, according to our results, we can assume that kidney preservation with simple surface cooling and initial wash through with the Collins' solution is at least as effective as permanent perfusion preservation.

Therefore, because of the simplicity and the low cost of the method, we think that it must be the one to use in kidney exchange programmes pending the development of newer and more successful preservation techniques.

ALEXANDRE: I think you should say that the longest preservation time is not 28 hours but 29 hours, because we received a kidney from Paris, preserved in Collins' solution with a total ischaemia time of 29 hours and the patient had no post-transplant tubular necrosis. I now give the floor to the champion of the other preservation methods, Dr Claes.

CLAES: I would like to talk a little about continuous perfusion. I want to stress some of the comments of Dr Kreis even further. There are two types of kidneys, those that are damaged by a pre mortem period of hypotension and warm ischaemia after cardiac arrest, and those kidneys removed under ideal circumstances with normal blood pressure and without any warm ischaemia at all. Both experimental and clinical observations have shown that the preservation of these two types of kidneys requires two different approaches. The same preservation methods cannot be used in both instances. Figures 7 and 8 show experimental results with a Gambro machine. Figure 7 shows 96 hours' preservation with this machine; I think this is the upper limit for

![Graph](image-url)

Figure 7. Serum creatinine of five consecutive dogs after 96 hours continuous perfusion and immediate contralateral nephrectomy
preservation of undamaged kidneys. Using the same techniques but with one hour warm ischaemia, we found that the upper limit for damaged kidneys was 48 hours of perfusion (Figure 8). Even so renal function was not normal 14 days after transplantation. Forty-eight hours is the upper limit for damaged kidneys perfused continuously. Figure 9 shows kidneys stored by simple hypothermia for less than 10 hours (mean 6 hours), up to 16 hours (mean 12 hours), and with simple albumin perfusion (mean 20 hours). I would like to
Figure 10. Frequency of immediate onset of function in human kidneys after storage by simple hypothermia and continuous plasma and albumin perfusion.

Figure 11. Frequency of immediate onset of function in human kidneys when taken after spontaneous cardiac arrest, after respirator switch off and on 'beating heart'.
remind you of Dr Kreis's figures from the Paris material, where 35% of kidneys stored from zero to two hours had immediate function and 46% of those stored for 9 to 16 hours functioned immediately. We have compared our results of perfusion in damaged and undamaged kidneys, using the perfusion machine. Those Swedish kidneys removed with a considerable warm ischaemia time have an immediate start of function in 90% of cases. Those kidneys obtained mostly from Oslo from beating-heart donors also functioned immediately in 90% of cases. This compares favourably with Kreis's figures of 50% although his kidneys were stored for a mean period of 20 hours, the longest preservation time being 40 hours. I would like to show you comparisons between the different preservation methods for damaged, or a mixture of damaged and undamaged kidneys.

Figures 10 and 11 show the results from kidneys with immediate function. There is a considerable difference between those stored by simple hypothermia for less than 10 hours and longer than this time. Of those stored for less than 10 hours only 7% started immediately. In the albumin perfused group there was an immediate start of function in 50%.

When comparing kidneys perfused between 10 and 20 hours with those perfused between 20 and 40 hours, there is no difference in the frequency of immediate function. Dr Kreis has also told us that perfusion machines are complicated, bulky and heavy. Gambro have developed a new machine (Figure 12).
which is small enough to be placed on an aeroplane seat. The membrane oxygenator is incorporated in the unit. We have used this for ten human kidneys with the same good results as with the old Gambro machine. We have also preserved dog kidneys for the similar lengths of time.

ALEXANDRE: I think we can now start the discussion of these preservation methods. Some have advantages over others, and some have the virtue of simplicity. I would like to make some comments as we are at the centre of Eurotransplant and experience a wide variety of methods.

We have preserved more than 80 kidneys on the Belzer machine at our own centre and transplanted them using the Belzer's criteria. We have also received and transplanted kidneys preserved on the Gambro machine, with plasma and with albumin, as well as kidneys preserved with Collins' solution, and I must say that my own conclusion is the same as the assistant surgeons. They find that the Collins' method has simplicity and lets them sleep in peace during the night whilst the refrigerator keeps the kidney in good shape for the following day. It is very difficult to be simpler than that. I am very surprised to see the length of time you have been able to preserve kidneys with the Gambro machine. With the Collins' solution the longest preservation time has been 29 hours as compared to 40 hours on the Gambro machine as I recall. I would like to hear what Dr Jakobsen has to add, and how he is preserving kidneys in Norway.

JAKOBSEN: We are of course very influenced by Gothenborg results and we have Gambro machines. At the local hospital when we remove the kidneys they are immediately perfused with a Collins' solution and a transport medium of bicarbonate with 10% sugar solution. Then the kidney is packed in a sterile container prefabricated by Nunc, Denmark (Figure 13) and transported in a box with freezing elements. We have these sets in all the peripheral centres. When the kidney arrives in Oslo we put it onto the Gambro machine for perfusion. We may then transport the Gambro machine by plane to the hospital where the transplantation is to take place, or leave it on the Gambro machine for daytime transplantation. Since we have had the Gambro machine we have not transplanted any patient during the night. We considered this quite an advantage.

SCHIPPER: I should like to state that even a small Gambro and small Belzer machine, both of which can be seen in the Industrial Exhibition, will not be the solution for the transport problem of organ transplantation because the machine needs someone to accompany it and then it has to be sent back; it will result in difficulties with Customs, flight reservation problems, and people being sent on emergency flights without return tickets. The present preservation time either with Collins' solution or preservation machines
allows you to do what is necessary with the kidney; however we have another goal to achieve, a preservation time of more than 5 days in order that we can gain an advantage from the results of MLC tests.

CLAES: In Gothenborg we have perfused 300 human kidneys, of which we have sent 80 away. We are now sending the kidneys almost exclusively on scheduled planes thereby reducing the cost of transportation. We are also sending the machines without an attendant. We leave the machines completely alone at night relying on them to continue the perfusion. Considering the cost mentioned by Dr Kreis and the problem of trying to reduce it, we have been able to reduce the overall costs of transplantation, since the increased frequency of immediate start of kidney function has markedly decreased the need for post-operative haemodialysis. So that at least in our centre although the cost of perfusion is higher than that of Collins' solution, the total cost of transplantation has decreased.

KREIS: Actually I am not sure that the high frequency of renal failure we observe in France after transplantation is due to the preservation techniques. I think many other factors can play a major role, especially the way the donor is treated and the treatment given to the recipient just before revascularisation of the kidneys. We are now trying new protocol using Lasix, but at the moment we have too few cases to speak about. However, up to the moment there has been no failure even after long preservation of the kidneys.

ALEXANDRE: You mean you treat the transplanted patients with Lasix?
KREIS: Yes, we treat the recipients just before revascularisation of the kidney.

CLAES: We are not pre treating our recipients and we still have 90% immediate function. Out of the 24 or 27 kidneys received from Oslo some of the donors were pre treated whilst others were not.

J BOELAERT (Paris): May I ask Dr Claes if he has an explanation for the better results he obtained after using continuous perfusion with an albumin solution rather than by Belzer's plasma?

CLAES: I can only guess at the explanation. Albumin is a very standardised solution, whilst the electrolyte content of plasma changes from one batch to another. There are also some immunological considerations that might play a role in plasma. You might have cytotoxic antibodies from the blood donors which may affect the kidney; these are absent in the albumin solution.

BOELAERT: Does the albumin solution you use for continuous perfusion contain fatty acids?

CLAES: Yes, quite a lot. It contains three times as much lipids as plasma.

G OPELZ (Los Angeles): I would just like to make a brief comment. Dr Claes has shown data that a higher rate of immediate function was obtained with machine perfusion than with cold storage. This is the opposite to what we found. One thing we looked into later was to compare the survival rate of kidneys that had immediate function with those with delayed function. We could not see any difference. I wonder if anyone has other experience. We think that whether there is immediate or late function does not necessarily matter for kidney transplantation.

CLAES: Yes, we have compared our machine perfused kidneys with kidneys stored by simple hypothermia. Of those stored by simple hypothermia the 6 months' survival rate was 55% if they were stored for less than 10 hours; if they were stored for more than 10 hours only 35% functioned 6 months after transplantation. Of the machine perfused kidneys the same number were functioning 6 months after transplantation. But there was a very big difference in the function of these kidneys; only 25% of those stored by simple hypothermia had normal renal function, while 45% of those stored by machine perfusion had normal serum creatinine.

M PAPADIMITRIOU (Thessaloniki): I should like to ask two questions of Dr Claes. First, what happened to the Gelin type of solution with rheomacredex: