Panel on the Maintenance of Life in Uremia*

DAVID M. HUME, Moderator

Dr. David M. Hume (Stuart McGuire Professor, and chairman, department of surgery, Medical College of Virginia, Richmond): I'd like to begin by asking Dr. Doolan a question. Do you have any special technique or criterion, Dr. Doolan, for determining the reversibility of disease in a patient that is being dialyzed for acute renal shutdown? That is to say, how do you decide whether to turn the dialysis off after several days?

Dr. Paul D. Doolan (director, clinical investigation department, Naval Medical Research Institute, Bethesda, Maryland): I don't know if I understand this question.

Dr. Hume: Well, suppose you've got a patient with acute shutdown and you have dialyzed him, because you had to keep him going. How do you decide whether this patient is going to "open up" sometime on his own; how long do you keep dialyzing him if you don't have a chronic program, and when do you decide that the shutdown is irreversible?

Dr. Doolan: If he's got acute renal failure, I don't know whether you can ever say it's irreversible. This question seems to emerge when you have shutdowns of unknown origin, and you are wondering about whether the person doesn't have acute glomerulonephritis, for example. If they don't open up in less than 30 days, then the likelihood of their opening up is very remote.

Dr. Hume: How do you decide they have got acute glomerulonephritis?

Dr. Doolan: Well, I think history and clinical appraisal is all I know of.

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If an adult is shutdown with acute glomerulonephritis, the prognosis is poor. I think it varies among different people as to when you feel justified in doing renal biopsy to see whether or not this will help you with making the decision of whether to continue dialysis. I would say that, in my own experience, renal biopsies have not helped.

Dr. Hume: Anybody else on the panel want to comment on this question?

Dr. John E. Kiley (professor of medicine, Albany Medical College, Albany, New York): I think when you see a patient with acute renal failure that does not open up after two or three weeks, you begin to see a somewhat characteristic behavior on the part of the physician handling the case. What we tend to do, first, is to support the patient by dialytic means, hoping that diuresis will ensue. But once you go into the second or third week, one certainly begins to feel pushed. After having eliminated any obstructive uropathy (by cystoscopic examination, etc.), we then do a renal biopsy. And, although there are some contraindications to doing a biopsy, it has been helpful in revealing a disease condition that we had not suspected, e.g., glomerulonephritis, overwhelming pyelonephritis, and infarction of the kidney. These conditions tend to make one turn off the dialyzer, because this is not acute tubular necrosis, and the kidney will not regenerate. The other thing to do would be to put a catheter up by way of the femoral artery to the level of the renal artery and inject a radioopaque dye. In this way, one can study the vascularity of the kidney. In some instances we have discovered that there has been bilateral infarction which we didn't suspect. This usually occurs when the patient has infarcted one kidney, say a year or two earlier, without its being clearly diagnosed, and later the patient has infarcted the other kidney. So, renal biopsy and pyelography can be helpful, when, after a month of dialysis you're beginning to wonder whether you are not rapidly going into chronic dialysis, inadvertently. Perhaps someone else on the panel has had more experience than I with the use of the newer diagnostic techniques of infusion pyelography.

Dr. Hume: Some patients don't "open up" for 60 days. The question is, at the end of 30 days, what do you do?

Dr. Belding H. Scribner (chief, division of kidney disease, department of medicine, University of Washington, Seattle): We're obviously confronted with this problem continually, because we do have a chronic program that is full. But at the same time, we are in a very serious dilemma in this kind of situation. I underscore completely what John Kiley says about the use of the biopsy at the 30-day point, so to speak. The other side of the coin here is, if you do find normal glomeruli and tubular necrosis at 30 days, then you are committed to keep the patient going on dialysis indefinitely. I know of one patient from Stanley Sheldon's group in England that went 90 days with tubular necrosis and then opened up. So, on the hopeful side, if you do come up with this diagnosis on renal biopsy, even in the presence of anuria, then you are obliged to go on. If you are worried about the vasculature, I think the aortogram may be done in 60 days or 90 days, if you are still "sitting" on the case. I can not elucidate the question Dr. Kiley raised about the newer radiographic techniques.

Dr. Joseph H. Magee (director of renal section, department of medicine, Medical College of Virginia)[1]. I want to allude to what Dr. Scribner just said. One of the abstracting journals had reported two cases of cortical infarction, where dialysis was carried out for 70 to 80 days before recovery. The authors believed that some one-sixth or one-fifth of nephrons, which are juxtamedullary, will come back and function if you dialyze them long enough. So I wonder if you aren't on the griddle for about two to three months, where shock or cortical infarction might have been the cause of shutdown.

Dr. Hume: Would anybody on the panel like to tell about his experience with the use of large quantities of contrast material, or would anybody like to comment on the use of radioactive materials, renal scans or radiorenograms, as assists in determining whether renal artery thrombosis has occurred—Dr. Kiley?

Dr. Kiley: Well, of course, I can't see how the use of radioactive substances is going to help you, because they don't really reflect the blood flow, but rather the ability of the tubular cells to concentrate and excrete the isotope. These patients may have neither blood flow nor secreting cells, so I would not be enthusiastic about these procedures.

Dr. Hume: If you have neither blood flow nor kidney cells, you wouldn't get any uptake, but if you have got some uptake, then that would be some evidence of vascularity.

Dr. Kiley: If you're looking for vascularity, I still think that renal angiography would be beter than isotopes.

Dr. Hume: Dr. Kiley, in your earlier discussion (paper on artificial dialysis in adults), you talked about using dialysis for hypercalcemia. I am wondering if you would advocate this form of therapy in hypercalcemic crisis, rather than operating on a patient who has hyperparathyroidism and hypercalcemic crisis, and removing his parathyroid adenoma. Another condition I noticed on your list was ammonia intoxication, and I wonder how your results have been with this.

Dr. Kiley: Well, first, I'll put my guard up by saying that at that time I was showing a list of situations which have been recorded as successfully treated by dialysis. Now, with hypercalcemia, we have an interesting situation there. I have not personally treated a hypercalcemic crisis by dialysis, so I am in no position to disagree with Dr. Glenn's[2] statement that parathyroidectomy is preferable. However, as

[1] At present, assistant professor of medicine, Jefferson Medical College, Philadelphia.

[2] Dr. James F. Glenn, professor and chairman, department of urologic surgery, Duke University, had spoken earlier on surgery in the prevention of uremia.

a surgeon, I would like to strike back by asking you if this would not be an extremely difficult type of emergency operation. The hypercalcemia may be due to hyperactivity of the parathyroid, which is deeply situated within the body. I think the complexity and difficulty of this surgery is at least a factor suggesting that dialytic therapy might be more efficacious; it is certainly more straightforward. How do you feel about this operation itself?

Dr. Hume: We have not had much experience with this. We had one patient who we thought had this problem. He certainly had a hypercalcemic crisis, and we dialyzed him for a short while, with some fall in calcium, although its level did not fall strikingly. We then took the patient to the operating room, explored the neck and then made the diagnosis of widespread metastatic disease, which hadn't shown up in x-rays. The patient ultimately died of malignant disease. Dr. Magee, do you recall that patient? I've forgotten exactly what the results of dialysis were.

Dr. Magee: I think we got calcium down from about 20 to 18. We just dialyzed for minimum number of hours and weren't getting anywhere and proceded with the operation. Thomas and co-workers[3] in a review of about 14 such cases, said they believed the thing to do was to get them right up to the operating table, because you just can't dialyze fast enough.

Dr. Kiley: Well, I would disagree with that. I think that if you are equating a good operation with relatively poor therapy, that certainly is true, but I also think that there are better medical ways of managing this disorder than by dialysis. As a matter of fact, I think dialysis may be weak, because you are dealing with a double equilibrium caused by abnormal parathyroid hormone, so you will have calcium coming out of the skeleton just about as rapidly as you can dialyze it out. On the other hand, by the use of sulphate and citrate, and, at least theoretically, EDTA, you can cut down considerably on the amount of ionized calcium that is present. This kind of medical therapy, although a temporary measure, can give you a good deal of time, even in the middle of the night, to prepare the patient and the operating room for surgery. And it can forestall the disaster that sometimes occurs with sudden death. So, I wouldn't minimize the usefulness of the right kind of medical therapy.

Dr. Doolan: I don't know whether it was a tribute to Dr. Kyle, my old boss, but I never saw a hypercalcemic crisis with hyperparathyroidism, and he had only a few cases. I have seen hypercalcemic crises with metastatic bone disease. This is the case in which you are not worried about operating. You can lower calcium by giving these people steroids, or you can lower it by doing peritoneal lavage, and, if you want to, you can put EDTA in the peritoneal lavage solution and remove even more calcium that way.

Dr. Hume: That's a good thought. Actually, there have been about 40 of these reported in the literature and the mortality is about 50%.

Dr. Doolan: With the hyperparathyroid?

Dr. Doolan: Yes.

Dr. Magee: And there are a lot more now.

Dr. Doolan: Well, my only point was, they're not all surgical.

Dr. Hume: No, not right away. We get them in the end, though, because there is no medical cure for hyperparathyroidism.

Dr. Doolan: The discussion has spun around how fast the patient with hypercalcemia should get to the operating room. But, what about the hypercalcemia that is not due to hyperparathyroid?

Dr. Hume: Well, we don't take those to the operating room.

Dr. Doolan: This is why I mentioned peritoneal lavage, steroids, and EDTA in the peritoneal lavage solution.

Dr. Hume: It is true that the majority of the hypercalcemic crises that we have seen here have been due to carcinoma of the breast, and we usually treat those with steroids to get them off the hook. Now, Dr. Kiley, I would like to ask you about dialysis in ammonia intoxication.

Dr. Kiley: We demonstrated quite a few years ago that the ammonia ion is very efficiently removed by a dialyzer, and we have used this with some gratifying results in about half a dozen patients. The thing I want to emphasize is that I don't believe at all that this is effective clinical use of dialysis. Ammonia toxication is almost invariably handled better by other approaches.

Dr. Hume: Were these people in hepatic coma, or were they people who had ingested some household detergent?

Dr. Kiley: The patients who were successfully treated were patients with portal cirrhosis who were getting along quite well, who then had a massive gastrointestinal hemorrhage. The hemorrhage was then stopped one way or another, but they went into ammonia intoxication from digestion of the blood in the gastrointestinal tract, and they were benefited by the removal of this excess ammonia. But I think this has very little practical general clinical worth.

Dr. Hume: Dr. Kiley, when I was an intern and resident, we used to see patients with various types of renal shutdown and potassium intoxication. In those days, a major indication for dialyzing a patient was potassium intoxication. We used to go scurrying around trying to get the patient just on the razor's edge, watching for EKG changes of potassium intoxication. And we were in sort of a sweat to see whether he was going to survive, and to judge the right moment to put him on the kidney. Now you suggest in your talk that we ought to get an EEG instead of an EKG, to decide when to put the patient on the kidney. This is harder to get than an EKG, and it is somewhat more difficult to interpret. Do you really feel that this is the way to decide when to put a patient on the kidney?

Dr. Kiley: Well, first of all, let us be clear that the EEG has nothing to do with potassium intoxication. Although I was possibly skipping along to catch up a little time, I did preface my slide of the EEG with the statement that

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[3] Thomas, W. C., Jr., J. G. Wiswell, T. B. Connor, and J. E. Howard. Hypercalcemic crisis due to hyperparathyroidism. *Am. J. Med.* 24: 229–239, 1958.

it was not generally available. And I would agree with your comment that, were this to be efficiently used, it must become more available clinically, and I think we must work more to that end. We have it fairly available now because this is a particular interest of ours. We have a portable EEG machine which can be taken to the ward, and you can count the frequency of the waves per second as they come off the machine. So, the EEG can become clinically useful, and I think it is something we must progress with. Really, what we are striving for here is a relatively simple electronic counter which will sort the seconds into two stacks; those in which the wave frequency of the EEG is above six and those in which the wave frequency is below six. The latter is a clearly abnormal situation. I do think that all of us are now using the EKG for potassium intoxication, particularly since the cardioscope has become generally available. If we have a potassium problem, we move the cardioscope into the room and turn it on and monitor the EKG continuously.

Dr. Hume: I was wondering, since Dr. Scribner has demonstrated that dialysis is so easy to do in the basement, why don't you simply dialyze the patients repeatedly when they have uremia, rather than rely on some particular danger signal to put them on dialysis?

Dr. Kiley: I think you're quite right, and I think that this is where we should be going. And, we should be using the artificial kidney and other dialyzers more as the human kidney, to preserve normalcy, rather than to correct a very abnormal situation. But I think that, in the present state of our knowledge, the main question is just how much dialysis is ideal. We just don't know that, because we have not yet correlated the changes in metabolism, particularly nitrogen metabolism, with these physiological changes. The thing I like about the EEG is that for the first time, we have something reasonably objective in altered physiology which we can use in clinical uremia. I was all sort of up-in-the-air in clinical uremia because we usually stood at the foot of the bed and looked at the patient, and wondered how sick he was, and that is hard to go on.

Dr. Hume: Dr. Finberg, I wonder if in the course of dialysis for poisons of one sort or another you ever see a rebound phenomenon after the dialysis is done. That is, the patient wakes up from dialysis and then, sometime later, he lapses back into coma. Has this ever been a problem?

Dr. Laurence Finberg (chief, division of pediatrics, Montefiore Hospital, and professor of pediatrics, Albert Einstein College of Medicine, New York): In most of the common poisonings that we see that is not a problem. There are some poisonings in which that has been notoriously reported to be the case. Then, you have to go back and dialyze again.

Dr. Hume: Dr. Finberg, supposing you have a problem, as occasionally comes up, that a child is born without kidney function. Is there any effective way to dialyze the newborn baby, or otherwise to manage the problem?

Dr. Finberg: Yes, I think there are two comments pertinent to this question. One is that the infant is probably the only living organism that can survive without any renal function at all, and without any artificial aid, for long periods of time. The record is up to six weeks. This is because the infant is so rapidly growing that if the absence of urine formation is not a consequence of some kind of disease which in itself induces katabolism, he will grow, and will so expand his body fluid compartments that they can actually hold the toxic substances in them in so dilute a form as to permit growth. This will be true if the infant is on the proper feed, and the ideal feed for this is human-breast milk. And that is how the record was set. The mother took her baby home, who subsequently turned out to have no renal mass at all. She didn't bring him to the hospital, not thinking it was terribly important that he hadn't put out any urine, until he was almost six weeks old. As for dialysis in infants, you can dialyze small infants if they have an abdominal cavity that is approachable. You can do it with peritoneal dialysis, of course, and this is what we talked about before. I am told the McNeal-Collins kidney can be adapted for small infants, but I haven't actually seen it in action myself. The other, larger devices are almost impossible to use on a small infant, even with trying to cut down the coil area and exteriorized blood volume.

Dr. Hume: Has anybody on the panel dialyzed a child under two years of age?

Dr. Scribner: Dr. Robert Hickman, in the department of pediatrics in Seattle, has been working on the problem. It seems to me the number-one requirement for infant dialysis is a small stable external circuit. I think Dr. Hickman has dialyzed a child only four weeks old, and he is using the Kiil half-length, one-layer unit, with a completely rigid external circuit, and no blood pumps. It is about a quarter the size of the unit we use for adults. If you fully prime the external circuit, the infant's vasculature cannot tell when he is on or off the dialyzer. The big problem in dialysis is to shift the blood from the equipment to the small child and back again. With a small rigid external circuit, we've had good luck in infant dialysis.

Dr. Hume: Do you put the child on a set of scales to be sure how much weight he is gaining or losing?

Dr. Scribner: It isn't necessary unless you're filtering large amounts of salt solution and then, of course, it's very helpful to have him on a scale. As far as the blood shift is concerned, if you have a rigid external circuit that is small and fully primed, there's no problem with bloodshift.

Dr. Hume: Dr. Magee, I wonder if you want to comment on some of the things Dr. Scribner has mentioned briefly, that is, the medical management of a patient with chronic uremia who is not yet ready for dialysis?

Dr. Magee: Picking out some of the things the speakers have brought up today, the common situation now is that practically no uremic patient comes in on the ward about whom you are not asked whether there is some reversible feature. Twenty-five years ago there were no nephrologists because there was nothing for them to do. Most people didn't believe for 100 years after Bright's description of

uremia that there was any such thing as reversible uremia. The things that seem to have come along to have changed all this were: 1) Weiss and Parker[4] showed that pyelonephritis was a common cause of chronic uremia. They picked out, retrospectively, a lot of reversible cases that came in with a pericardial friction rub or uremic frost, and then left the hospital. Some of the older physicians didn't think they'd ever seen this but here there were some cases. 2) The salt-losing nephritis emphasized by Thorne and colleagues[5]; when the patients went into shock, instead of giving them adrenocortical hormones you only had to give salt. 3) Then along came the exponential growth of blood banks and non-exponential growth of technicians and we had a large number of transfusion reactions. A lot of younger fellows really got going from the encouraging experience of bringing some of these patients through. These easy ones are not seen any more, but they just reinforced the concept of reversible uremia. 4) W. J. Kolff's book, *New Ways of Treating Uremia,*[6] which had the artificial kidney in it, but most importantly, it had the high-caloric, low-protein feedings and the protein-sparing feeding, and the necessity of restricting water, to avoid pulmonary edema. 5) And then came the electrocardiogram and the flame photometer, which helped tell us when the potassium is elevated.

Dr. Hume: I would like to make a couple of comments relative to Dr. Scribner's talk comparing chronic dialysis and transplantation, and then ask him to comment on my remarks. In the first place, I think we all ought to admit right off the bat that some form of chronic dialysis is essential to any transplant program. That is, without Dr. Scribner's help, and without the use of his device, our own program might never have gotten off the ground. Secondly, transplantation is not a therapeutic program at the present time; it is an investigative program. It's difficult to talk to Dr. Scribner without being challenged by him, because he regards chronic dialysis as a therapeutic program. This immediately puts you on the defensive. So, I'd like to point out the insufficiencies of chronic dialysis, and correct a few figures that have been given about transplantation. 1) The patients who were cared for by him for chronic dialysis were a highly select group of intelligent people. It is not everybody who can go down in his basement and dialyze himself. At least ¾ of the patients we have done transplants on, not only couldn't dialyze themselves, they barely had the intelligence to void! Our overall objective has not been to see what percentage of survival we can get, but what we can learn about transplantation. 2) Chronic dialysis is pretty much out with respect to children because it does interfere with growth and sexual maturity, as Dr. Scribner has said. 3) The number of patients who can be benefited by chronic dialysis is very small. Suppose for a moment that you were to take the point of view that the present objective of either of these two methods is to keep the greatest number of people alive. (Although this is not the point of view that we take, it is the point of view that Dr. Scribner takes.) In his own setup in Seattle, Washington, he has had six patients on hemodialysis in a five-year period; five of the six patients are still living. He's done six patients on peritoneal dialysis; five of these patients are still living. And he's got two patients in their basements. That's a total of 12 patients in five years, who are living who would otherwise have died. Our own program of transplantation has been going only two years. We have 28 patients living who would otherwise have died. None of Dr. Scribner's patients is cured; they all still have their disease. None of his patients is really well, but this is not true of any of the transplant patients either. 4) Hypertension does occur in patients with chronic renal disease, even in those on a low-salt diet. We have seen this in two instances out of the 50 patients we've had on chronic dialysis. Dr. Scribner hasn't seen it in his six patients, but it does occur, and it is a problem and one that you cannot solve with dialysis but you can solve with transplantation. 5) The degrees of independence of the two types of patients, that is, the patient with kidney transplant and the patient on dialysis, are quite different. Even if dialysis is done in the basement, and even if you can dialyze yourself at night while you sleep, it does encroach upon your independence to a greater extent than does the normally functioning kidney transplant in a well patient. 6) None of the patients on chronic dialysis really ever regain their pre-sickness weight. They do regain some weight, but they never are as healthy as the patients with good transplants, although not all patients with transplants have good ones. 7) Almost all of the patients on chronic dialysis require blood transfusions which are expensive and dangerous. 8) Neuropathy is almost never corrected by chronic dialysis—hemodialysis, that is. 9) The mortality figures are somewhat misleading. If you take Dr. Scribner's figures and show them on a slide today, 71% of the patients on chronic dialysis are now surviving. This figure is not too different from the figure for the larger series of transplant patients. Sixty-two per cent of all the patients we have done from the very first one are surviving. Of all transplants from related donors in the three largest groups in the country, 73% are surviving. Of our own cadaver transplants, 70% are surviving; and if we took only our last eight months' cases—93% of those are surviving. Even if we took all the patients we did in the first year, all of whom are now one or two years post-transplant, 46% are still living. Four of the first six patients we did are still living, and the two that died, died of total body radiation, which we no longer use. Virtually all of our patients have been on chronic dialysis before transplantation, and all of them prefer the transplant to chronic dialysis. The

[4] Weiss, S., and F. Parker, Jr. Pyelonephritis: its relation to vascular lesions and to arterial hypertension. *Medicine* 18: 221–315, 1939.

[5] Thorn, G. W., G. F. Koepf, and M. Clinton, Jr. Renal failure simulating adrenocortical insufficiency. *New Engl. J. Med.* 231: 76–85, 1944.

[6] Kolff, W. J. *New Ways of Treating Uremia.* London: J. and A. Churchill, Ltd.

figures which Dr. Scribner quoted, i.e., that 70% of identical twins who could have lived five years had died of the disease of the host, are figures that were reproduced in a recent editorial,[7] and are incorrect. The facts are 80% of all twins done in the last 10 years are living at present. Although it has been reported that occasionally either the twin kidney or a homografted kidney has developed the disease of the host, this has not happened as a rule, and it has not happened in any of our homotransplants or any of those in Denver. There's something more than 100 cases in this combined series, so, I think it must be extremely rare. He quoted Dr. Don Thomas' thoughts, namely, that he figures that 5 to 20% of patients who were transplanted had a chance of living two years, and that less one percent of them had a chance of living for four years. Dr. Thomas has recently moved to Seattle and it is understandable that he would have these thoughts. Dr. Scribner is a very convincing fellow. Had Dr. Thomas thought otherwise he might be carried away in the middle of the night. The actual figures from the largest series in the country are that, of those patients who could have lived from one to two years, 40 to 45% are living. Of our own patients who could have lived for two years, which is a very small group, 50% are still living. Dr. Scribner also says that the dialysis program works without doctors. But the patient with basement kidney must have about $1,500 a year in professional fees. Furthermore, in our own dialysis unit, which is modeled after Dr. Scribner's, Dr. Bower hasn't had a vacation in a year. Even though our program is run by nurses and technicians, Dr. Bower doesn't leave town for any length of time. I would like to conclude these remarks by saying there is really no competition between chronic dialysis and transplantation because the goals of the two are vastly different. But, I think if there is going to be an ultimate solution to the problem, that the patient with a normally functioning kidney, urinating in a normal fashion, with a completely normal life, who feels perfectly well, and has regained his pre-sickness weight, is in a little better situation than the fellow with a home kidney in the basement. Dr. Scribner, would you like to comment on this?

Dr. Scribner: I guess we could stay around a couple of hours and really have at it, but time is over already. I'll just make one or two brief remarks. We only had 12 patients at the University of Washington because it was not our job to take all the patients that could come our way. Our job was to demonstrate the feasibility of the method, to get on with the job of doing research to improve the method, and to learn all we could about the biochemistry of what's going on. Actually, unless we have had a new research project, such as the home program, we have not added a patient to our program in over two years. In contrast, of course, the new center downtown now carries 13 patients and is about to go up to 30, so the statement that there are fewer patients being benefited by chronic dialysis is simply a function of economics. If we had the money, we could take everybody in King County and we think we are going to be able to do this soon with the combination of the center and the home program. One or two other points. To say that 80% of all twins done are now alive is not necessarily contradicting the statement that 70% of the twins who could have survived five years are now dead.

Dr. Hume: This statement is incorrect.

Dr. Scribner: This was the statement that Don Thomas got from the group in Boston about two weeks ago. I do believe that chronic dialysis, based on our experience, is an accepted method of treatment. This is borne out by the world survey that we have just conducted. In this survey we asked, "can any well-trained internist, if he wants to, maintain a patient on chronic dialysis?", and all 20 investigators said yes. So, chronic dialysis is no longer an experimental technique; it is a therapeutic technique available to anyone who wants to get in, roll up his sleeves, and go to work. The problem is that we need time to activate the units, we need money, and proper facilities. And, incidentally, with all due respect to the excellent program here (at the Medical College of Virginia), they do not have proper facilities for chronic dialysis on an outpatient basis. The chronic dialysis program here is solely for the support of the excellent transplant research program that is going on.

Dr. Doolan (to Dr. Hume): You mentioned something about someone overpowering someone. I would find it hard for anybody to overpower you, Dave. There really wasn't any argument the way you wound it up, in that nobody argues with the ultimate desirability of having an intact kidney in you. But, let me ask you, how many transplants with non-maternal donors have survived over a year?

Dr. Hume: Of the patients that started off with a non-maternal kidney that could have survived more than a year, there were two, and they are both alive. Of the patients that have received cadaver kidneys, an unrelated group, 70% are still alive.

Dr. Doolan: After one year?

Dr. Hume: No, because they haven't all been a year.

Dr. Doolan: Dave, will you make the statement here and now that you, a surgeon, can guarantee a more than one-year survival of 50 or 70% in unrelated homotransplants?

Dr. Hume: Of course not, that would be a ridiculous statement to make.

Dr. Doolan: Well, boy, you threw around an awful lot of statistics. I don't know whether you are talking about two weeks, two months, or what.

Dr. Hume: Well, I think the most important figures in this regard are that if you take the patients who have been done more than a year ago, who are still living at the present time, so that all of these patients are from one to two years, and are patients who couldn't have lived more than a year, 46% of them are living.

Dr. Doolan: Would you give me that once more? I'm a little slow.

[7] Elkinton, T. Russell. Moral problems in the use of borrowed organs, artificial and transplanted. Annals int. Med. *60:* 309–313, 1964.

Dr. Hume: Yes. Take the patients done in the first year of our program. Our program began August, 1962. All those patients are now from one to two years from their transplant. Now take all the patients who could have lived during that time—there were 13 such cases who were done during that year —six of those patients are now living, which is 46% of the group. If you take those patients who have now been one year, which is not quite the first year, all told, 44% of patients who could have lived during that year are now living.

Dr. Doolan: I would only say that, as far as I know, unrelated transplants is strictly an investigative technique and if you select your patients well, from what I know of the Seattle group, it's a therapeutic technique. So, the only position I'm left with here is wondering why you have the sensitivity you do in the first place.

Dr. Hume: I have no particular sensitivity. I think that the figures do represent the facts as they are now. I think it's important to feel that transplantation results are good enough to justify any investigation on this program. And I think it's good that the results of hemodialysis are not so good that one should settle for this type of therapeutic regimen at the present time. That's all.

Dr. Scribner: I don't wish to give up keeping score here, but could I take advantage of this situation to ask you to comment on what the fundamental improvements have been in the technique of transplantation in the past year or two. I have a feeling that things are improving.

Dr. Hume: I think the thing we've perhaps observed better than before are, first of all, that at the first indication of rejection, immunosuppressive therapy is increased. Secondly, I think the use of local radiation has helped and I think this may be one of the reasons that our cadaver transplants are coming along better than some. This is something that has come out of the laboratory that seems to help clinically. Thirdly, the use of prednisone has been extremely valuable in preventing rejection. Fourthly, the preparation of patients for surgery by the types of chronic dialysis now available is vastly better. We started off with peritoneal dialysis and now we use the Scribner technique. Fifthly, I think that keeping the patients on hand longer has given us the time to observe them and manage them better after transplant.

Dr. Doolan: May I make one more comment in a different vein, Dave, and that touches on statistics. I recommended for the military section of the AMA that the treatment of post-traumatic renal insufficiency should be prophylactic hemodialysis à la Seattle group technique, which I think is the finest available. The way I justify this statistically is that Scribner and Bob Hagstrom are the only ones that have lowered mortality rate in acute renal insufficiency in the post-traumatic group. To the best of my knowledge, that's where the issue stands statistically at the moment.

Dr. Scribner: I'm terribly biased in this regard, but I feel that the prophylactic approach to acute renal failure just makes eminent good sense as Paul just very well stated, and since dialysis in a properly-run center such as you have here in Richmond is virtually without risk, and uremia is dangerous to a person with fractures and so on, it just is the only way to do it.

Dr. Hume: Thank you very much for your kind attendance.

"The basic texture of research consists of dreams into which the threads of reasoning, measurement, and calculation are woven".

Albert Szent-Györgyi, *Introduction to a Submolecular Biology*. New York and London: Academic Press, 1960, p 1.