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New Horizons for Radiologists Lecture

Introduction of Lecturer, Thomas E. Starzl, Ph.D., M.D.[1]

PHILIP J. HODES, M.D.[2]

COMPARED to the past, selection of this year's New Horizons Lecturer was easy. Once it was decided that the subject would be "Organ Transplants" we tried immediately to commit Doctor Starzl. Happily for all of us he was available.

Doctor Starzl was born in Le Mars, Iowa, in 1926. This makes him forty-three years old; thus he falls under the 45-year-age limit we try to require of all New Horizons Lecturers.

After his graduation from Westminster College in Fulton, Mo., Dr. Starzl went on to earn his M.D. and his Ph.D. degrees from Northwestern University in 1952 and 1954, respectively. From 1955 to 1956 Doctor Starzl worked at the Johns Hopkins University where his primary interest was in cardiovascular physiology and surgery. After two years as a resident in Surgery at the University of Miami, Doctor Starzl returned to Northwestern as Assistant Professor of Surgery. In 1964 he was called to the University of Colorado as Professor of Surgery where he is at this time.

Doctor Starzl has been the recipient of numerous honors including Achievement Awards from the University of Lund, Westminster College, and Northwestern University. He is author, co-author, or contributor to 21 books and more than 225 articles in the literature. The scope of his interests and activities is attested to by the fact that in 1968 and 1969 alone he published a total of 50 articles, most of which have been concerned with organ transplants.

Of additional interest is the fact that Doctor Starzl's Curriculum Vitae records with care and exactitude and sequentially all meetings in which he has played a major role; these number over 200.

There is not much more that I can tell you about Doctor Starzl. From his Dean and friends I learned that he is married, has three children, and loves skiing and swimming. The man works twenty-four hours a day every day of the year. Medicine alone is the prime drive of his life.

I am privileged, ladies and gentlemen, to present the Head of the University of Colorado team which has performed about one-half of all the world's reported liver transplants, Doctor Thomas E. Starzl, Professor of Surgery, University of Colorado Medical Center. His New Horizons Lecture for this year concerns "Organ Transplantation in Radiology."

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[1] Presented at the Fifty-fifth Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 30–Dec. 5, 1969.

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Thomas E. Starzl, M.D., Ph.D.
New Horizons for Radiologists Lecturer, 1969

Radiology and Organ Transplantation[1]

New Horizons for Radiologists Lecture

THOMAS E. STARZL, Ph.D., M.D., JEAN J. VANHOUTTE, M.D., DONALD W. BROWN, M.D., JOHN TAUBMAN, M.D., JOHN C. STEARS, M.D., MARVIN L. DAVES, M.D., and CHARLES G. HALGRIMSON, M.D.

ABSTRACT—The discipline of Radiology has played an indispensable role in the development and clinical application of transplantation procedures. The contributions have included radiotherapy, diagnosis, and research. In this communication, some of the wide-ranging activities of radiologists are reviewed, as these have been seen in a large transplantation program.

INDEX TERMS: Heart, transplantation • Immunity • Kidneys, transplantation • Liver, transplantation • Radiotherapy • Transplantation

Radiology 95: 3–18, April 1970

WITHIN the last decade the field of organ transplantation has grown in a truly extraordinary way, to the point where meaningful extension of life has been consistently achieved with renal homotransplantation (11, 12, 14, 19, 22, 30) and sporadically accomplished with transplanted livers (3, 31), hearts (2, 28, 34), and lungs (7). The tremendous contributions made to such a development by the discipline of radiology may not be recognized by the majority of radiologists. Nevertheless, it is a fact that radiologists participate in every phase of a transplantation procedure, starting with the prospective donors and recipients, continuing in the postoperative period, and, in the event of death, ending in the autopsy room.

At the University of Colorado, a clinical transplantation program was organized on an interdepartmental basis in early 1962, and the first kidney transplant was carried out in March of that year. Members of our Radiology Department participated in the initial planning, and in the ensuing years they have developed special interests in the various aspects of the overall problem which will provide the basis for this communication.

RADIOTHERAPY

Total-Body Irradiation

Total-body irradiation was the first kind of immunosuppression ever systematically tested in man. In 1958 a recipient at the Peter Bent Brigham Hospital in Boston was given a kidney from his fraternal twin after prior irradiation (20). That man is still alive, as is another patient treated under similar conditions at the Hôpital Necker in Paris a few months later (12).

In our series of renal transplantations only one patient has received total-body irradiation. This 12-year-old male was given a total of 400 roentgens (Fig. 1) before and after a kidney was transplanted from his mother in 1962. Profound leukopenia was produced, from which he eventually recovered. The first kidney functioned for five and a half years and was then replaced with a second homograft. The patient is still alive with a total follow-up of more than seven years. After the early postoperative period of the first

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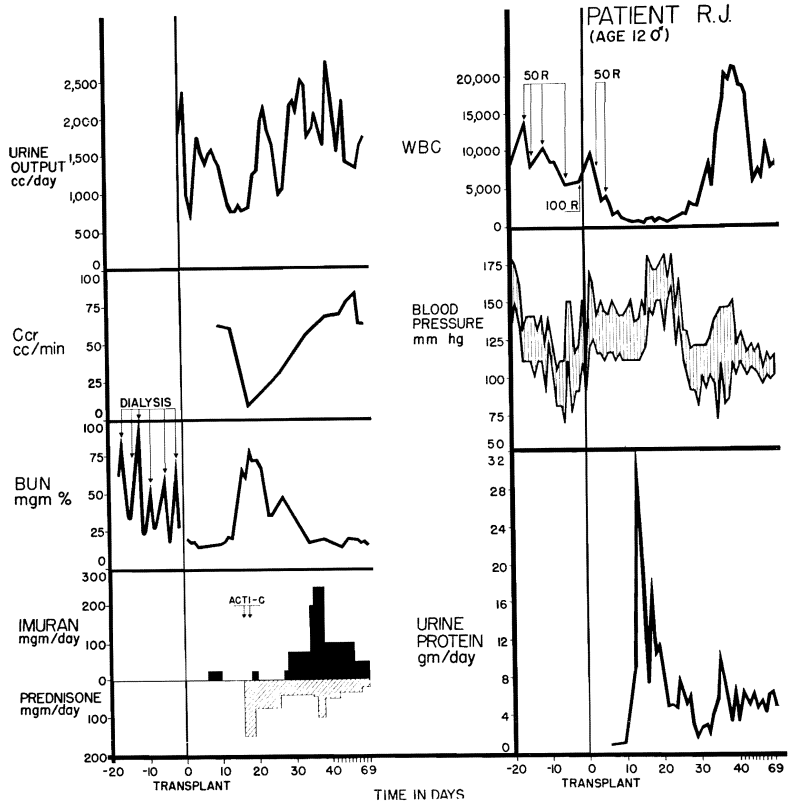

Fig. 1. Rejection crisis in a patient treated initially with total-body irradiation (400 R). Note transient oliguria, depression of creatinine clearance, and elevation of blood urea nitrogen, blood pressure, and urinary protein excretion. The changes were all reversible. The patient previously had undergone bilateral nephrectomy, splenectomy, and thymectomy. R, dose total-body irradiation; Acti-C, actinomycin C (each arrow equals 200 μg of actinomycin C administered intravenously). Imuran is synonymous with azathioprine.

These general events of rejection have occurred despite treatment with various therapeutic regimens used at this and at other centers. The homograft which was transplanted in 1962 functioned for more than five and one-half years. It then failed, and a second kidney was provided eighteen months ago with an uncomplicated recovery. (Reproduced with permission from Surg. Gynec. & Obst. **117**: 385, 1963.)

transplantation had passed, a conversion was made to treatment with azathioprine and prednisone (Fig. 1).

A number of lessons were learned from the study of this patient and in other early cases in which *only* drug therapy was used, omitting the radiotherapy. There is merit in considering the most crucial of these observations since they have been confirmed on many occasions, not only with the kidney but after transplantation of other organs as well. First, it was learned in this early experience that rejection was apt to occur even though the patient was under aggressive immunosuppressive treatment. In the irradiated patient under discussion, this was manifested by a secondary deterioration of renal function starting after about two weeks of excellent urine excretion (Fig. 1). The creatinine clearance fell precipitately at the same time as azotemia, massive proteinuria, and hypertension deepened. These adverse findings were all at least partially reversed by the institution of secondary steroid therapy (Fig. 1). This kind of demonstration by the clinicians added a new dimension to the biology of transplantation. It had become clear for the first time that rejection was a reversible process (9, 33), something that had never been appreciated on the basis of prior experimentation with animals.

The second key observation made in these first cases was that the intensity of immunosuppression required to control rejection very often decreased in the weeks

or months following operation. Thus, the patient whose course is shown in Figure 1 required relatively massive doses of prednisone early in his convalescence, but steroid treatment was subsequently stopped without deterioration of homograft function. In animal laboratories, it has been shown (21, 25, 27, 30–32, 35) that all treatment may be discontinued in some recipients of whole-organ homografts with survival for many years. We have observed examples of this kind of "graft acceptance" after initial immunosuppressive treatment with 6-mercaptopurine, azathioprine, and heterologous antilymphocyte serum. The period of treatment may be as short as several weeks or even several days.

It would be impossible to overemphasize the importance to the radiologist of these cyclic changes after transplantation, as will be discussed later on. The reason is that examinations are frequently performed during the first postoperative month to differentiate the events of rejection and its reversal from findings caused by other kinds of complications.

Other Uses of Radiotherapy

In spite of its historical importance, total-body irradiation is no longer used as a major form of immunosuppression. The reason is that the desired therapeutic effects depend upon a dose that is too often lethal. More discriminating irradiation, namely of the blood, has been shown by Cronkite and his associates (17) to mitigate homograft rejection, presumably by selectively killing circulating lymphocytes.

Also, many authorities recommend local irradiation of the graft, a suggestion first made by Dempster of London (6) and subsequently popularized mainly by Hume of the Medical College of Virginia (15). Hume routinely administers 150 to 200 roentgens per dose to kidney homografts on post-transplantation Days 1, 3, and 5. In controlled laboratory experiments the use of this measure alone can delay rejection (18), although the effect is rather minimal and unreliable.

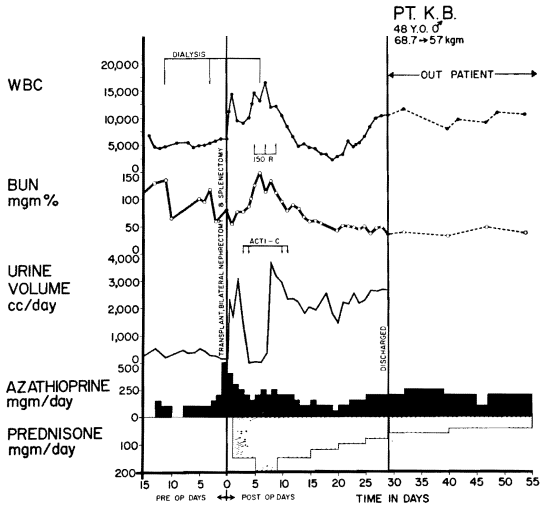

Fig. 2. Use of local irradiation to the homograft during rejection crisis. Three doses of 150 R (at depth) were given with a 250 kV unit. Homotransplantation was performed Dec. 4, 1963. Note the anuric interval, during which the irradiation was delivered. Renal function returned, and the kidney supported life for more than five years before it eventually failed and was removed. Reproduced by permission of Surgery **56:** 296, 1964).

Our own practice (30) has been to use graft irradiation only for an established rejection which cannot easily be controlled by other means. An example of this kind of case is shown in Figure 2. The patient had initial good renal function but he became anuric several days after operation at the same time as there was easily palpable swelling of his transplanted kidney. He was in intense pain which was promptly relieved with the first treatment of 150 roentgens delivered to the homograft. Shortly thereafter, urine excretion resumed, and he made an essentially uncomplicated recovery.

As more effective immunosuppressive regimens have been developed, and particularly with the introduction of heterologous antilymphocyte globulin (32), our need of local homograft irradiation has steadily declined until at the present time it is used in only 5 or 10 per cent of all cases.

DIAGNOSTIC INVESTIGATIONS

It goes without saying that a variety of general diagnostic examinations are carried

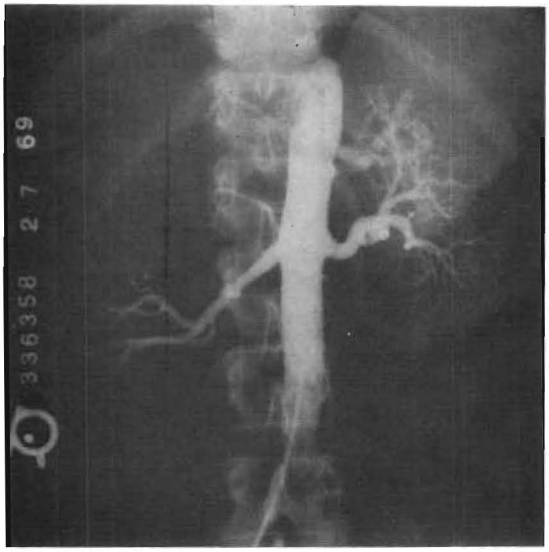

Fig. 3. Transfemoral aortogram in a prospective renal donor who was rejected from further consideration because of an unsuspected fibromuscular hyperplasia of the right renal artery.

out on all recipients and upon their donors. There is no point in going into these procedures except for some special considerations.

Donor Studies

Living Volunteers: With renal transplantation the best results have been obtained with the use of healthy consanguineous donors. If such a donor is to be considered, it is mandatory that an exhaustive medical work-up first be carried out. After all other examinations (including intravenous urography) are completed and found to be satisfactory, aortography is performed. There are 2 objectives; the first is concerned with the safety of the donor. It is surprising how often an unsuspected lesion of the kidney or its blood supply is detected.

An example is shown in Figure 3. This woman was an asymptomatic volunteer who was found to have fibromuscular hyperplasia of the right renal artery. She was rejected because of the known propensity of fibromuscular hyperplasia to occur bilaterally, for which reason it was feared that the same kind of lesion might later develop in her normal left renal artery. On the other hand, suboptimal kidneys may be accepted even with abnormalities as serious as intrarenal arteriovenous fistulas (Fig. 4). In the donor whose renal arteriogram is shown in Figure 4, the presence of the fistula and also the existence of a normal vascular system of the contralateral kidney were established by 2 aortograms taken five years apart. The organ was transplanted and functioned perfectly.

Of course, the second consideration in performing aortography is to anticipate technical problems that might jeopardize the recipient. Assessment of the vascular supply is a primary consideration but this is not always easy as is demonstrated in Figure 5. The left kidney was eventually proved to have 3 renal arteries and was not utilized.

Cadaveric Donors: The kind of assessment just described has been used in all volunteer living donors since the inception of our program. Until quite recently, however, it was not possible to have advance information about the blood supply of cadaveric organs. Many unpleasant surprises were encountered in the course of removing cadaveric liver or kidney homografts. A number of deaths occurred in our liver series which were directly attributable to complex and unsuspected vascular anomalies (31).

With the establishment of brain death criteria (1, 4, 5, 31), it has been possible to avoid these tragedies by means of donor angiography while an effective circulation is still present, a particularly important advance in liver cases. If a liver can be demonstrated in advance to have a single hepatic artery, the technical ease with which the operation can be performed is greatly increased.

Under similar circumstances of brain death, vasopressors may change the angiographic findings. The profound constriction, in the donor shown in Figure 6, of the distal arterial tree of various organs, including the liver, kidneys, and spleen, caused serious concern that the liver might

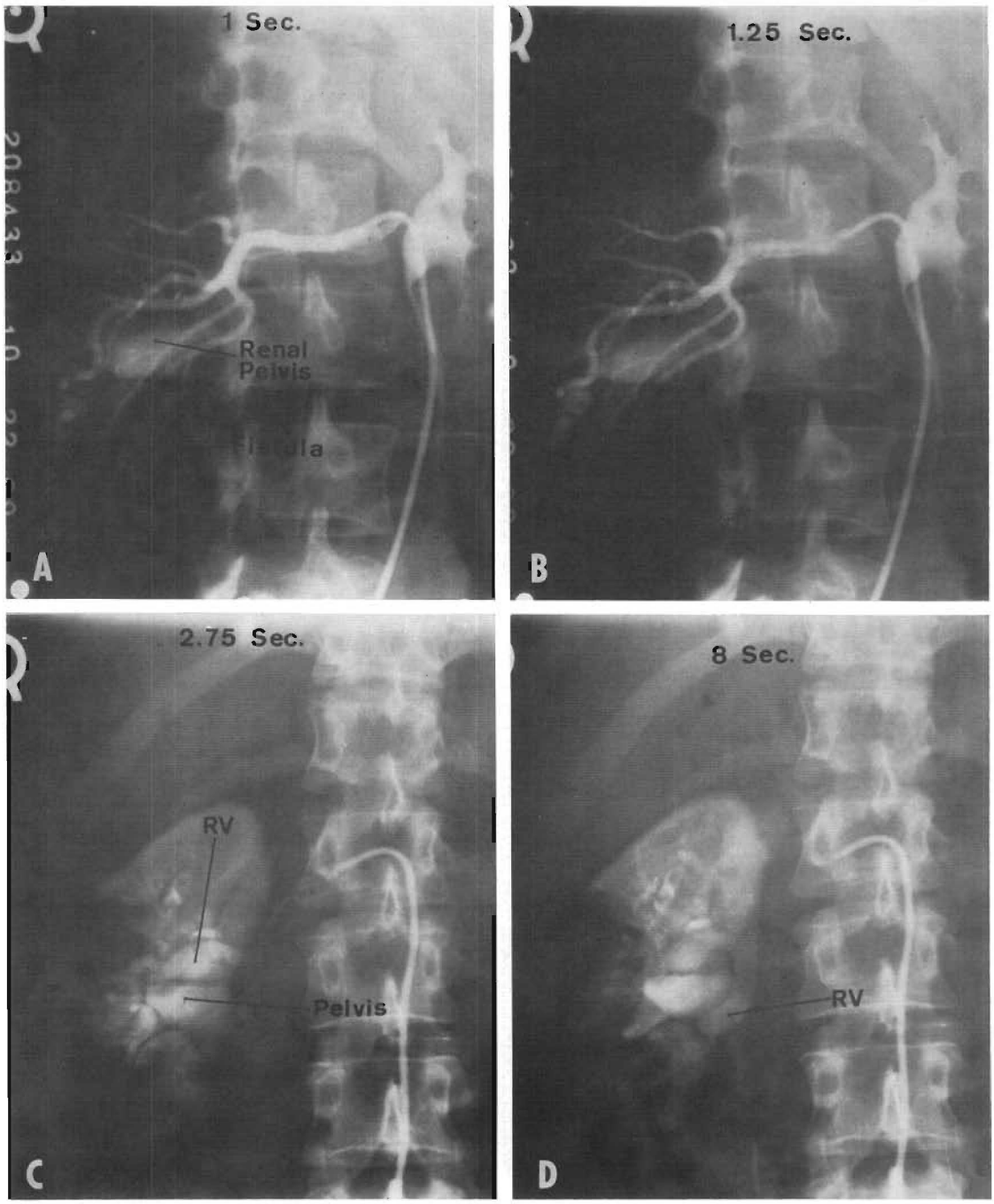

Fig. 4. Angiographic study of a right kidney which was eventually transplanted from a mother to her daughter.
A and B. Demonstration of an intrarenal arteriovenous fistula at some distance from the renal pelvis.
C and D. Later films show contrast material in the renal vein.

be unsuitable. Nevertheless, it was transplanted to a patient with intrahepatic biliary atresia and postoperatively it functioned well. That recipient has completely normal hepatic function now, two and one-half months post-transplantation.

In several donors, multiple hepatic arteries have been found by aortography.

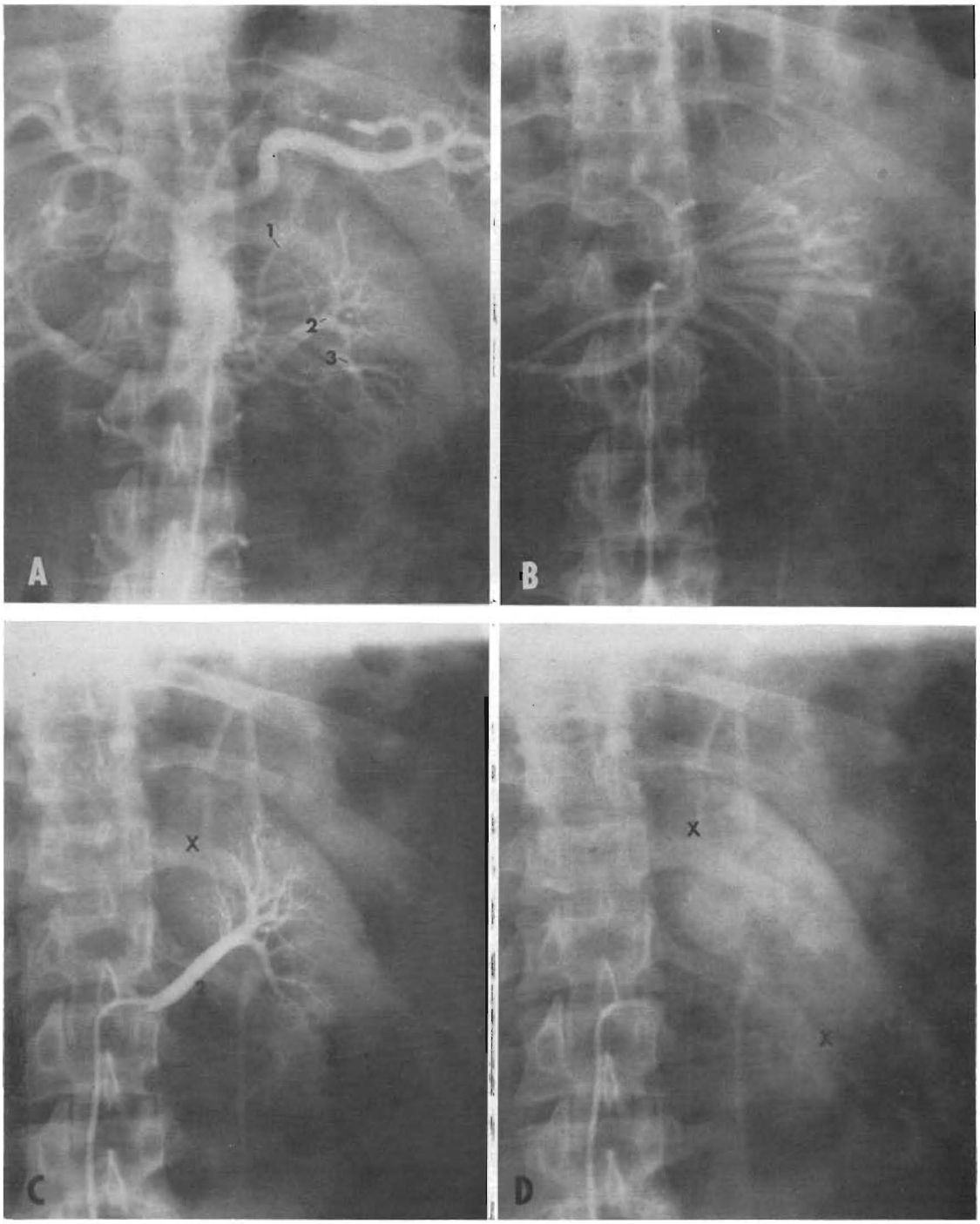

Fig. 5. Studies of a potential kidney donor. A. An aortogram showed what appeared to be multiple renal arteries to both kidneys. However, it was difficult to distinguish mesenteric vessels from what were thought to be 3 renal vessels (marked) passing to the left kidney.

B. A selective superior mesenteric arteriogram defined the pattern of the mesenteric arteries.

C. Selective left renal arteriogram of the largest or middle renal vessel. Note that contrast medium does not pass to either the superior or inferior pole (marked X).

D. Subsequent nephrogram shows nonvascularized poles.

In the case shown in Figure 7, the technical situation was thought to be too complicated to warrant proceeding and the organ was not used.

Recipient Studies During Rejection

At the beginning of this account, we mentioned the unstable situation that is typical after transplantation. Very often rejection necessitates for its reversal a striking intensification of immunosuppression. The clinician caring for such patients must be constantly attuned to distinguishing rejection from other complications, many of which are related to the toxic effects of immunosuppressive therapy. Of the antirejection agents, prednisone has probably been the greatest cause of morbidity (13, 24, 30).

Complications of Immunosuppression: One need do no more than show several examples of perforated peptic ulcers to illustrate the nonspecific complications that may occur in the early postoperative period. The patients are typically young and in the early weeks after renal transplantation. They characteristically have passed through a recent rejection crisis which was treated with an increase in steroid dosage. Perforation of a peptic ulcer can be surgically closed with eventual complete recovery. In cases like this an instant diagnosis is required if there is to be

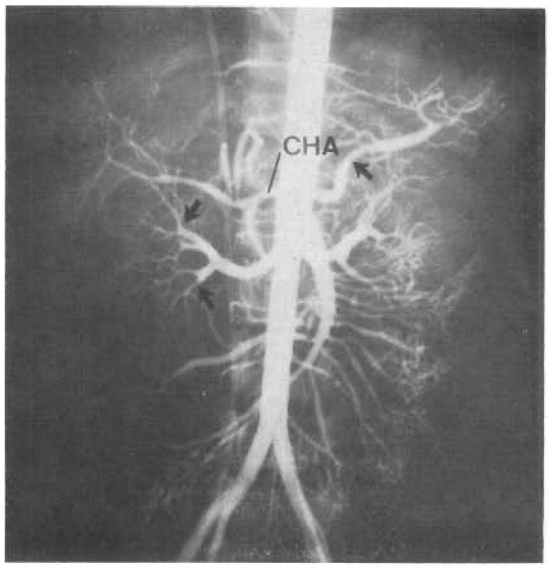

Fig. 6. Aortogram in a potential liver donor who had been receiving aramine in order to maintain a detectable blood pressure. The liver was supplied by a single artery. Note the areas of vasoconstriction (arrows) in vessels passing to the spleen, kidneys, and intestine. CHA, common hepatic artery.

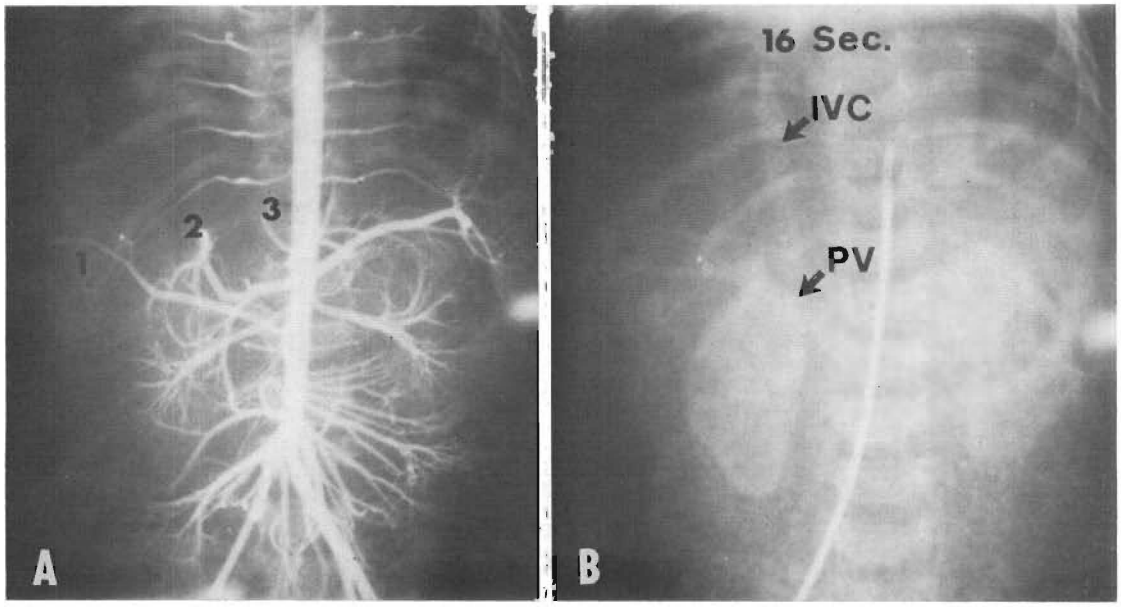

Fig. 7. Aortogram in a potential liver donor. A. The studies revealed multiple hepatic arteries arising from the superior mesenteric artery (1), the common hepatic artery (2), and the left gastric artery (3).
B. A late film (16-second) shows contrast material defining the portal vein (PV) and the inferior vena cava (IVC).

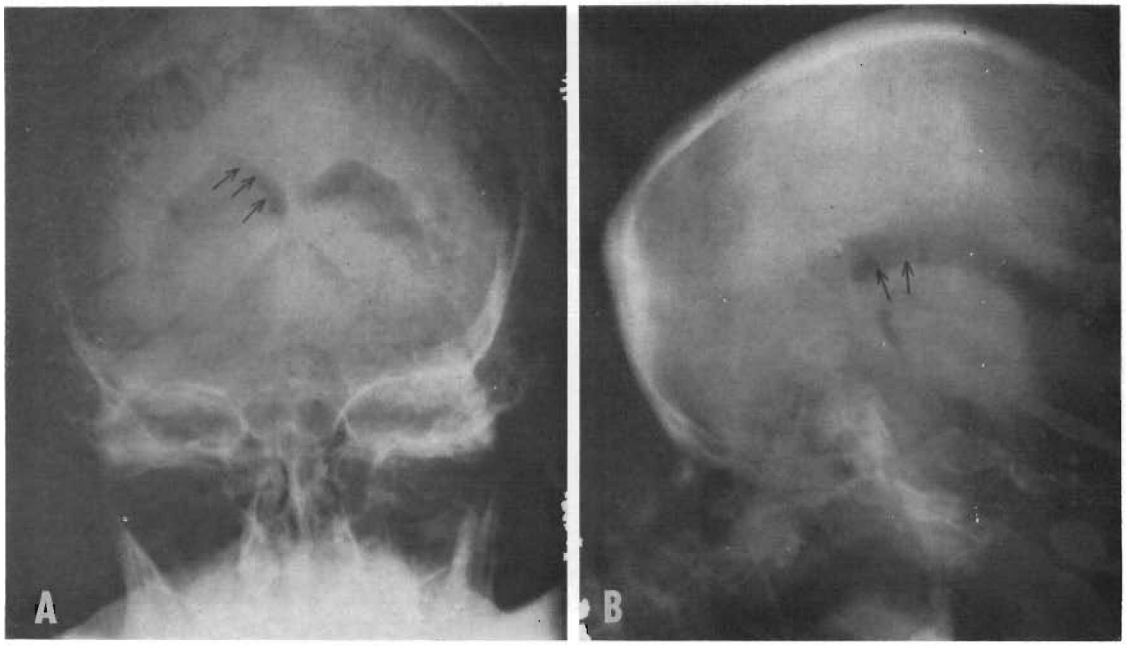

Fig. 8. A pneumoencephalogram in a 20-year-old woman who had been treated with renal homotransplantation a few months previously. Progressive hemiparesis had developed postoperatively. A mass was found, protruding into the right lateral ventricle. This was biopsied with stereotaxic apparatus and found to be a plasmacytoma.

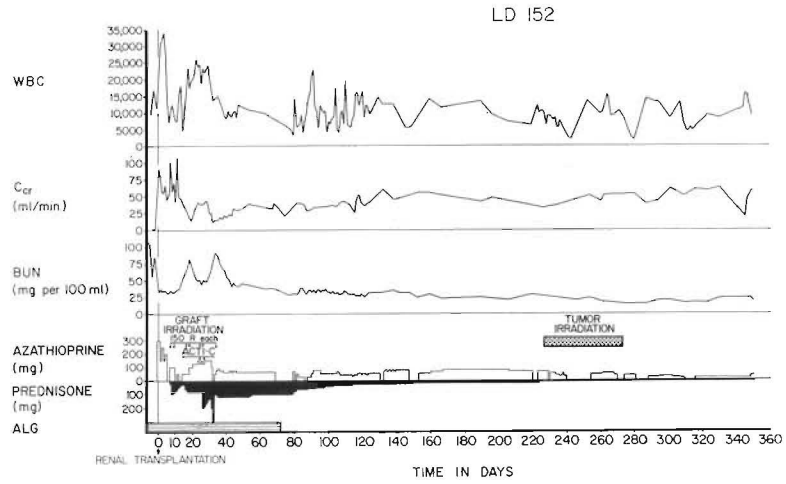

Fig. 9. The clinical course of the patient whose pneumoencephalogram is shown in Figure 8. When the diencephalic tumor was diagnosed, immunosuppression was drastically reduced, and the intracranial neoplasm was irradiated with a total of 5,650 R. Kidney function was well maintained, and tumor growth is apparently arrested since the patient has been well for more than two subsequent years.

any hope of survival. Peritonitis is a lethal event in the immunosuppressive patient unless the insult is of short duration. The diagnostic roentgenograms are of vital importance if operative intervention is to be carried out in time.

Numerous examples could be cited of the importance of the x-ray diagnosis in the treatment of other intra-abdominal calamities (23, 24), pneumonitis (13, 26, 29, 30), bone abnormalities (16, 30), and other disorders. There is no need to go into these in any particular detail beyond pointing out that certain diagnoses ordinarily regarded as rare are not especially uncommon in the transplant recipient. Radiologists

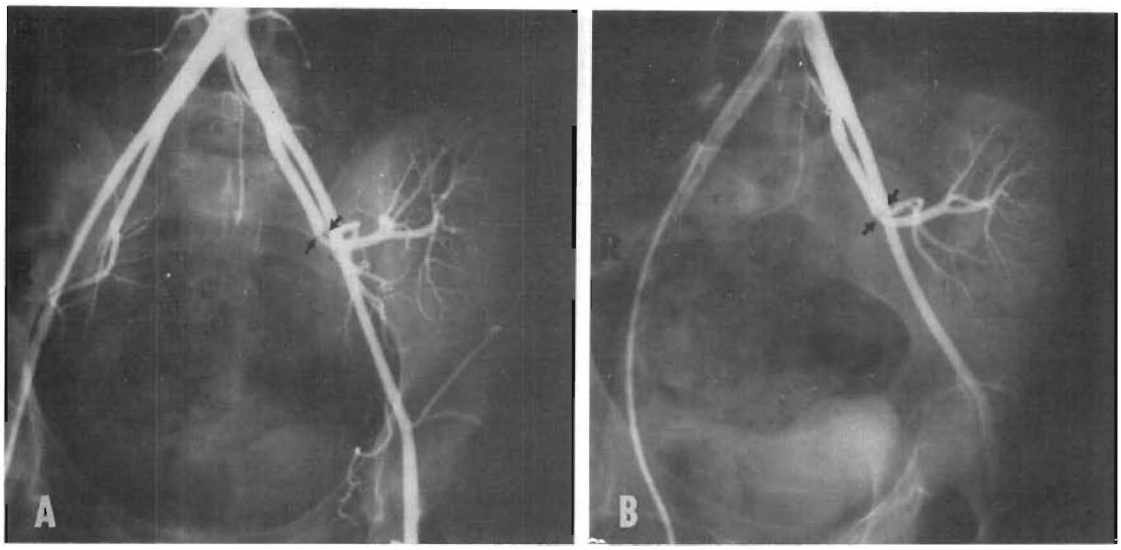

Fig. 10. Arteriogram of a renal homograft placed in the left extraperitoneal space. After transplantation, renal failure developed. The investigation reveals that both renal arteries underwent a high-grade stenosis at the anastomotic sites (arrows).

interested in transplantation probably see more examples of *Pneumocystis carinii* infection, a protozoan disease that in the past has been called plasma-cell pneumonitis, than they do of pneumococcal lobar pneumonia.

Intracranial disease has not uncommonly been noted in organ recipients. In one of the most interesting cases we have seen, the determination to establish a definite diagnosis averted what seemed to be certain death. The patient was a young college student with rapid development of progressive neurologic signs several months after renal transplantation. A cerebral angiogram was normal, but the pneumoencephalogram revealed a mass in the thalamus which impinged upon the lateral ventricle (Fig. 8). Under x-ray control a biopsy of this region was obtained with a stereotaxic apparatus, and the histologic diagnosis was made of a plasma-cell myeloma. Radiotherapy to the tumor was carried out at the same time as immunosuppression was markedly reduced (Fig. 9). The tumor apparently involuted. Renal function remained excellent despite the lightening of immunosuppression, and the patient has been well for the succeeding two and one-half years.

Technical Accidents of the Homograft: In addition to complications affecting the host tissues and organs, there may be problems with the homograft which do not have an immunologic etiology. An example would be compromise for mechanical reasons of the blood supply to the homograft (Fig. 10); in this renal recipient a progressive decline of kidney function proved to be due to stenosis of the two renal arteries which had been anastomosed separately. Another example was in a little boy who also received a kidney that had double renal arteries (Fig. 11, A). Postoperatively, good homograft function developed, but the patient became desperately ill with fever. After studies illustrated in Figures 11, B and C, a segmental resection of the infarcted portion of the homograft was successfully performed.

With renal transplantation the onset of secondary renal failure is sometimes due to mechanical defects of the urinary drainage system rather than to rejection. When this occurs, the diagnosis is heavily dependent upon radiologic techniques (Figs. 12 and 13).

Radiographic Studies in Rejecting Homografts: Many of the same diagnostic techniques used to prove or disprove the me-

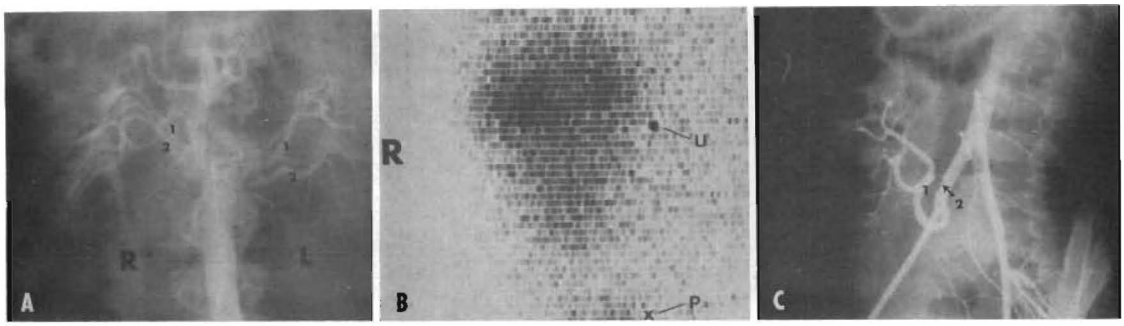

Fig. 11. Studies of a kidney before and after its transplantation. A. The aortogram in the paternal donor showed 2 renal arteries passing to each of the kidneys. The right kidney was transplanted.
B. After transplantation, the recipient became acutely febrile and hypertensive. A mercury scan showed a large defect in the inferior portion of the transplant which had been placed in the right extraperitoneal space.
C. An arteriogram in the recipient shows that the upper renal artery (*1*) was patent, but the site of anastomosis of the lower renal artery had become occluded. Partial nephrectomy was carried out.

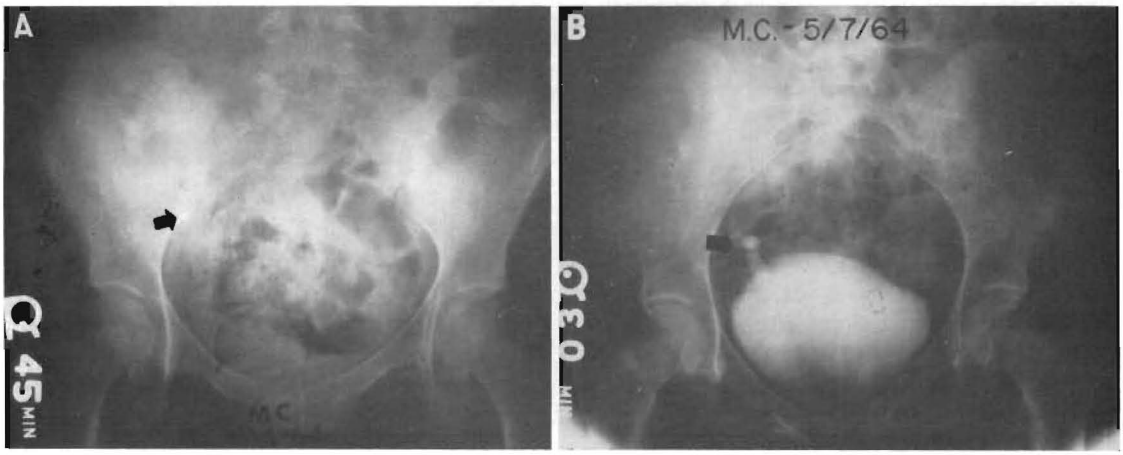

Fig. 12. Studies of a young woman who became suddenly anuric six months after operation. A. An intravenous urogram demonstrated a somewhat dilated pelvis with no visualization of the distal ureter.
The original urinary drainage had been provided by anastomosing the ureter to the patient's bladder. The patient was re-operated upon, and a ureter-to-ureter anastomosis was carried out with a satisfactory result.
B. After conversion to ureteroureterostomy, the patient's own ureterovesical junction was slightly dilated. Ultimately, the kidney was rejected and the patient died thirty-three months after transplantation.
The patient's renograms before and after the onset of obstruction were also suggestive of obstruction and its relief (Fig. 13).

chanical integrity of recently transplanted organs may play an even more important role in following the events of rejection under certain circumstances. With the advent of rejection, there is swelling of homografts and a reduction in their blood flow. This was first noted with kidneys, but the same also applies to livers and hearts. With hearts, for example, the appearance of cardiomegaly in the post-transplantation period is a serious sign. On the other hand, a series of films like those in Figure 14 are highly encouraging. The patient is a man who is well two and one-half months after cardiac transplantation. There has been a steady reduction in the size of the heart plus a striking amelioration of the visible signs of severe pulmonary hypertension that had been present prior to surgery. The pulmonary artery pressure before transplantation was 90 mm Hg and the correction of this abnormality postoperatively was very slow but progressive.

With liver transplantation the use of scanning techniques (8, 10, 31) provided crucial help in two ways. The first was to provide very objective measurements of

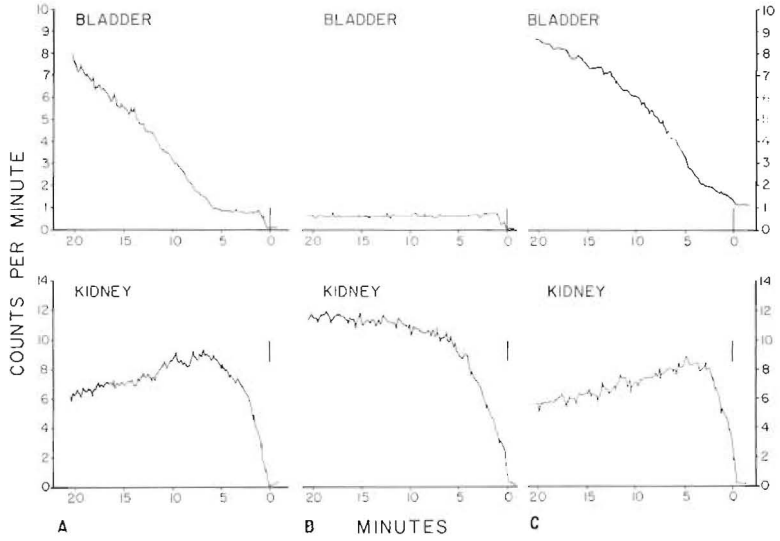

Fig. 13. Renograms obtained with ^{131}I orthoiodohippurate in a woman in whom ureteral obstruction developed six months after renal homotransplantation. A. Prior to the complication.
B. The patient has suddenly become anuric.
C. Two weeks after relief of the ureteral obstruction.
The intravenous urograms in this case are shown in Figure 12.

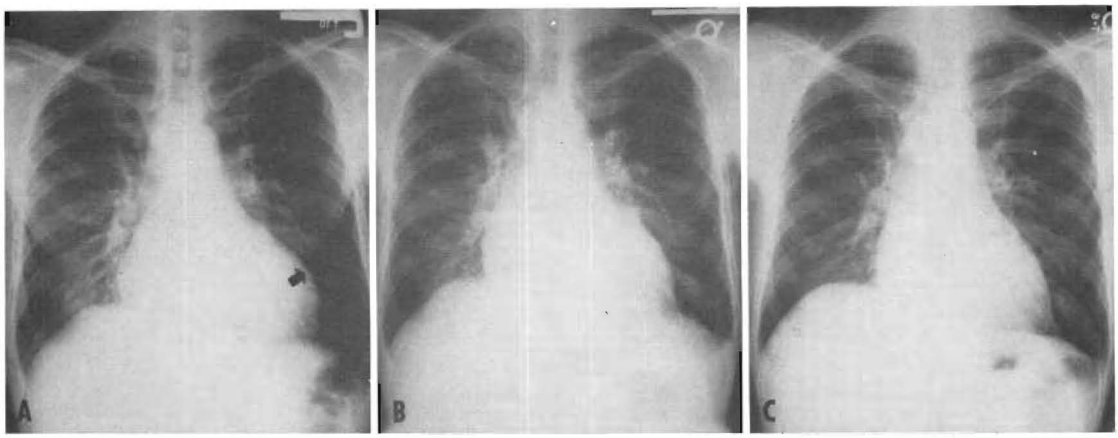

Fig. 14. Consecutive chest roentgenograms in a patient who eventually received an orthotopic heart transplant. A. In June 1969, the diagnosis of a ventricular aneurysm was made (arrow). Shortly afterward, partial excision of the fibrotic left ventricular wall was carried out.
B. In September 1969, the patient's condition worsened. The evidence of pulmonary hypertension seen in Fig. 14, A has increased. A few days later cardiac transplantation was accomplished.
C. Seven weeks after cardiac transplantation. Note the reduction in the size of the cardiac silhouette as well as a marked reduction in the pulmonary hypervascularity.

liver size. In Figure 15 a series of scans obtained with technetium 99m reveal progressive postoperative enlargement of the homograft. Although this patient had no definite deterioration of liver function, the homograft was passing through a rejection episode. After reversal of the immunologic crisis, the dimensions of the organ diminished.

Early in our experience with liver transplantation, the significance of these size changes was not appreciated and appropriate therapeutic adjustments were not made. The consequences were tragic as shown in Figure 16. This little child whose transplantation was for biliary atresia showed a remarkable increase in the size of the liver despite which secondary

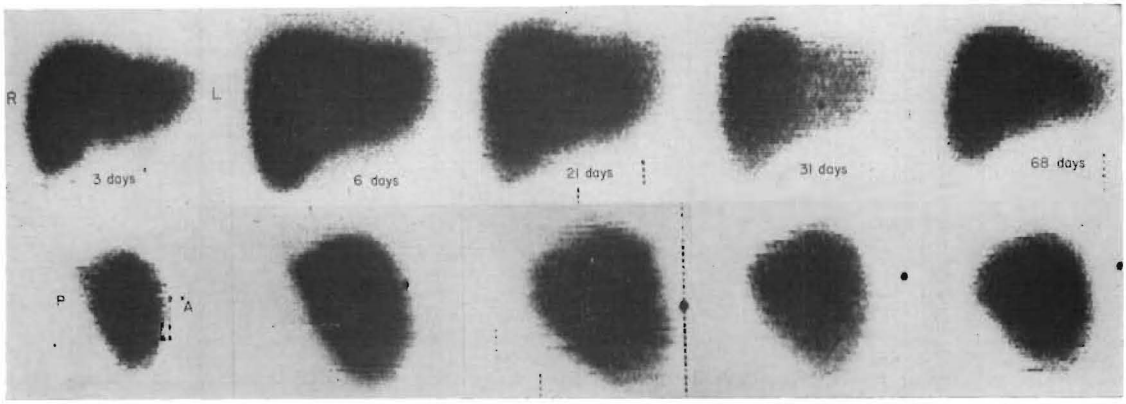

Fig. 15. Anteroposterior and lateral liver technetium-99m scans of an orthotopic liver homograft. In this 15-year-old patient, the diagnosis was hepatoma. He received the liver of a 6-year-old cadaveric donor. Note the remarkable liver swelling which occurred at the time of rejection (six days) and which lasted for more than two subsequent weeks. By sixty-eight days the anteroposterior view appeared to have returned to about the same dimensions as had been present shortly after operation. However, the lateral view showed that the liver mass was increased; liver function was then completely normal. Note that the pickup of the isotope remained homogeneous throughout the period of observation, except possibly at thirty-one days. More scans of this patient taken at the time of invasion of the homograft by recurrent tumor are shown in Figure 18.

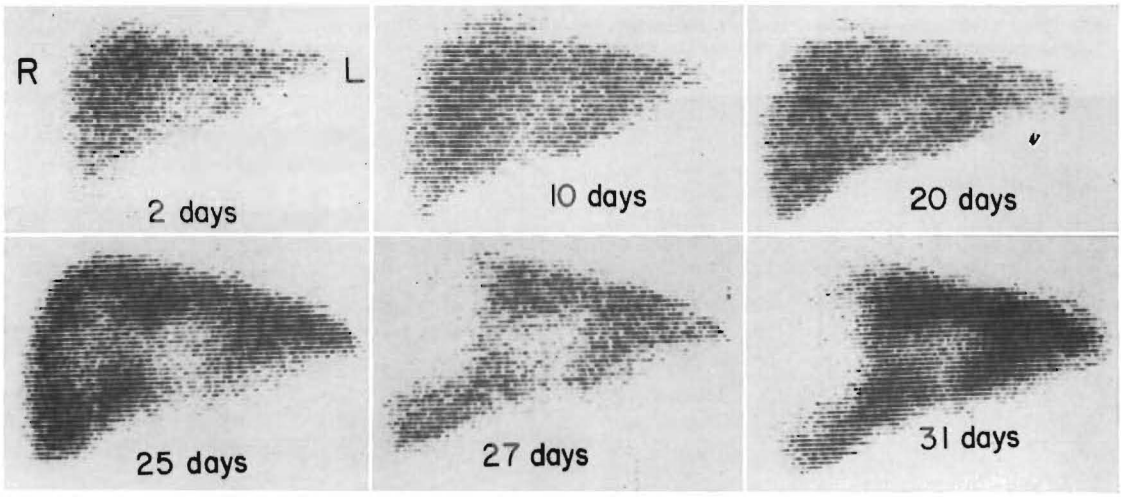

Fig. 16. Postoperative technetium scans in a child whose liver had been replaced because of extrahepatic biliary atresia.
2 days. The small homograft is normal.
10 days. An increase in size is evident, although the general configuration of the organ is still normal.
20 days. No further change is noted.
25 days. The examination was conducted as an emergency when gram-negative septicemia developed, with very high increases in the transaminases. Areas of decreased isotope-uptake are obvious in the right lobe and the central part of the liver.
27 days. A striking extension of the process can be seen less than 48 hours later. A debridement procedure was carried out the same evening.
31 days. Four days after debridement the radiographic appearance was improved.

jaundice did not develop. Ultimately large central portions of the liver became necrotic, apparently as the blood flow to the transplant fell below a life-supporting level (31).

As already mentioned, we believe that the essential explanation for this complication was that inadequate immunosupression was given. However, radiographic studies in cadavers showed that the technique we were then using for orthotopic transplantation could result in a nonocclu-

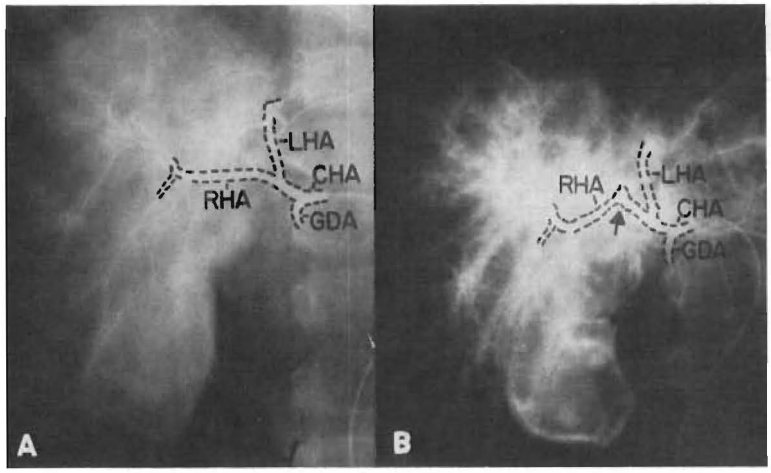

Fig. 17. Angiographic studies performed in a 5-year-old child immediately after her death from head injuries. Contrast medium was injected into the common hepatic artery (CHA) proximal to the gastroduodenal artery (GDA). A. Initial injection. Note the smooth course of the right hepatic artery (RHA).
B. The restraining ligaments of the liver have been incised, a cholecystoduodenostomy performed, and the head of the x-ray table elevated to 60°. The right lobe of the liver has rotated down and medially. The course of the left hepatic artery is undisturbed. However, the right hepatic artery (RHA) is now severely kinked where it passed beneath the common duct. See text for discussion. (Reproduced with permission from Ann. Surg. **168**:392, 1968.)

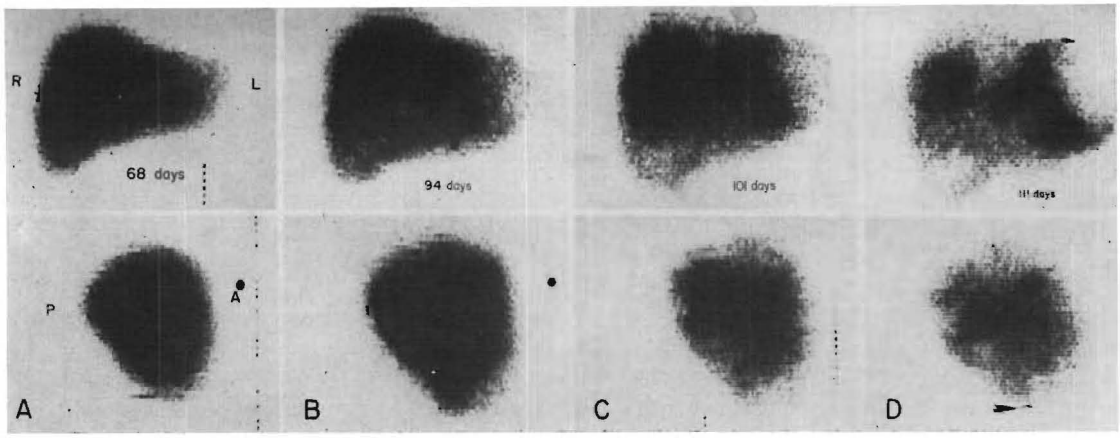

Fig. 18. Destruction of an orthotopic liver homograft by tumor recurrence in a patient whose own liver was removed and replaced because of a primary hepatoma. The case is the same one as portrayed at an earlier postoperative time in Figure 15. The postero-anterior and lateral liver scans were obtained with technetium 99m.
A. *68 days*. The scan is the same as the last one shown in Figure 15.
B. *94 days*. The patient had become jaundiced. Hepatomegaly is evident.
C. *101 days*. Multiple areas of poor isotope concentration are now visible.
D. *111 days*. The process has continued its rapid progression. By the time of death one month later, the homograft was almost completely replaced with carcinoma. Extensive metastases also affected the lungs and other organs.

sive kinking of the right hepatic artery (Fig. 17). On the basis of these studies a detail was added to the operation, consisting of resuture of all the suspensory ligaments of the liver (31).

Since correcting the deficiencies in immunosuppression and since making the change in surgical technique, we have not seen the complication of partial liver infarction.

LATE STUDIES

So far, this discussion has been mainly concerned with a variety of immunologic and nonimmunologic complications of the dangerous early postoperative period.

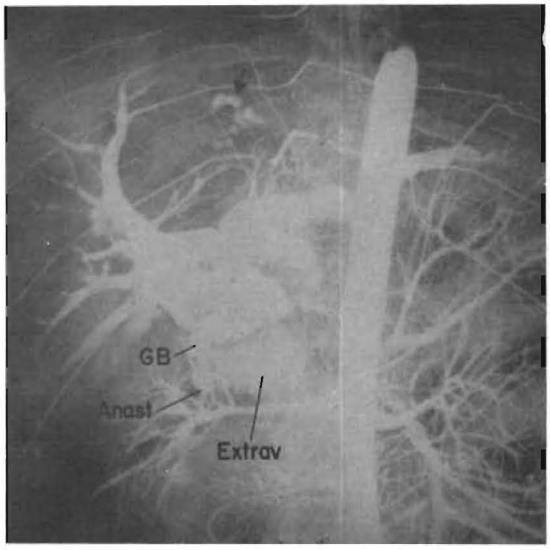

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Fig. 19. Postmortem cholangiogram in the recipient of an orthotopic liver transplantation that had been carried out almost one year previously. Biliary reconstruction had been with a cholecystoduodenostomy. The medium was injected through a catheter tied into the collapsed gallbladder (GB). Note the extravasation of contrast material (*extrav*) and general dilatation of the duct system. The correlation of these findings with the development of metastases is discussed in the text. The vascular shadows resulted from an aortogram. The artefact indicated by the arrow was caused by removing a parenchymal specimen.

Late studies are required less frequently, but they are nonetheless of the utmost importance. Furthermore, the nature of the investigations cannot always be anticipated accurately when new kinds of transplantation are carried out for the first time, as can be illustrated by the first trials with liver transplantation. Initially, a prime indication for this operation was thought to be hepatoma. Unfortunately, removal of the primary tumor in these patients did not prevent subsequent metastatic disease (31). Often, the transplanted liver eventually became invaded by metastatic hepatoma at an extraordinarily rapid rate even though it was thought that the initial excision had been complete (Fig. 18).

In other recipients whose original disease

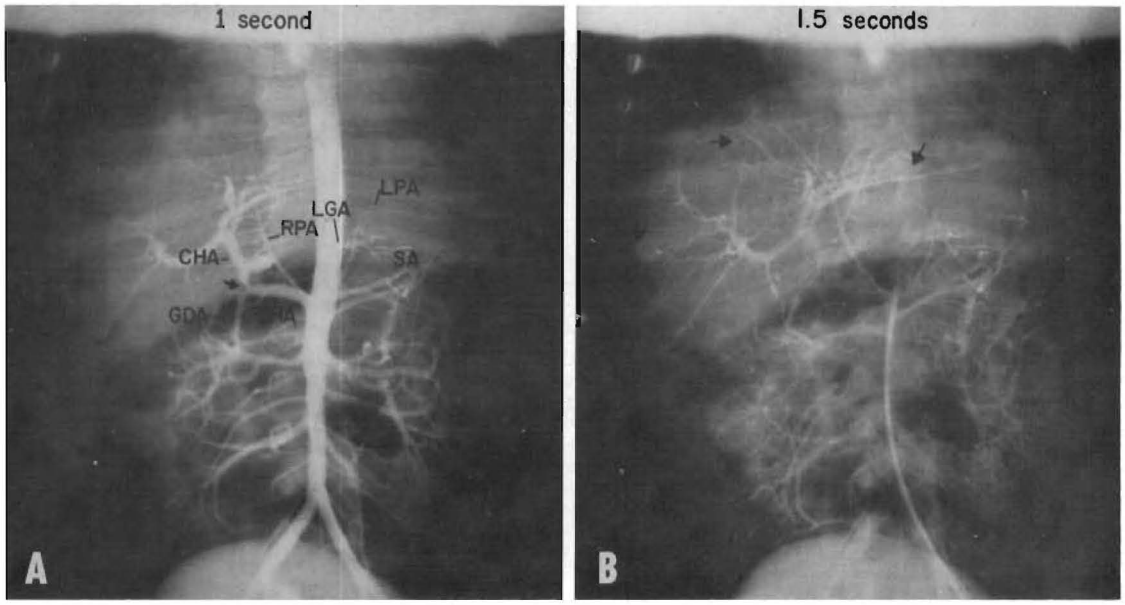

Fig. 20. Aortogram obtained 425 days after orthotopic liver transplantation for extrahepatic biliary atresia. Persistent low grade jaundice developed one year after liver replacement. The original arterial anastomosis had been between the host proper hepatic artery just beyond the gastroduodenal artery (GDA) and the homograft celiac axis. A. One second after injection, there is a stenosis (arrow) at or near the anastomosis. The small arteries are serpiginous and seem to communicate with lakes in some areas, suggesting intrahepatic arteriovenous fistulas. Note the large caliber of the right phrenic artery (RPA), probably as the result of its participation in a collateral blood supply. CHA, common hepatic artery; LGA, left gastric artery; LPA, left phrenic artery; SA, splenic artery.

B. *1.5 seconds after injection.* The terminal vessels are racemose. Accumulations of contrast material (arrows) suggest intrahepatic arteriovenous shunts.

was hepatoma, it has been possible to show by postmortem radiographic examinations how tumor metastases had affected the biliary system of the transplant (31). In the case shown in Figure 19, jaundice developed late in the postoperative course. At autopsy, almost one year after transplantation, a metastasis was found to have obstructed and eroded into the duct system, causing an extravasation. In all autopsies involving liver recipients, we believe that it is essential to study both the arterial and biliary duct systems of the transplants by radiographic methods before disturbing the homografts in any way. Some of the most incisive investigations about these cases have come from this kind of preliminary postmortem examination (31).

Parenthetically, it should be added that studies of the vascular and biliary systems during life are not infrequently required. In two instances, it has been necessary to perform operative cholangiography in order to determine if jaundice were due to mechanical obstruction of the biliary ducts or to late rejection.

Similarly, arteriography is sometimes indicated (Fig. 20). In this case, re-operation was not performed. The child is still in good and stable condition now almost two years post-transplantation.

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