

## Surgically Correctable Intra-Abdominal Complications Before and After Renal Homotransplantation

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IN CARING for 184 patients treated with renal homotransplantation during the last 6 years, the need has often risen to treat surgically a variety of nonurologic intra-abdominal complications. Some of these developed during pretransplantation dialysis, some were related in one way or another to the transplantation itself, many were the consequence of postoperative immunosuppressive therapy, and some appeared to have no relationship to the unique circumstances which surround the patient.

This communication describes the various abdominal problems excluding wound complications, which either led to surgical intervention, which were encountered as incidental findings at the time of transplantation or which were not diagnosed and operated upon but contributed to or caused the patient's death. In addition, the way in which standard surgical practices were applied to meet the needs of these high risk patients will be discussed.

### Methods

There were 184 recipients from 3 to 55 years of age. All but one required initial resuscitation with either peritoneal dialysis or hemodialysis. The renal homografts were obtained from blood relatives, nonrelated

volunteers, or recently deceased subjects, in that order of frequency. In more than 90 per cent of cases the patient's own diseased kidneys and spleen were removed through an upper abdominal incision on the same day as the homotransplantation; in almost all others nephrectomies and splenectomies were performed either before or afterwards. All but a few homografts were placed into the extraperitoneal space of the iliac fossa through an oblique lower abdominal incision. A special transperitoneal approach was used for homograft insertion in small children.<sup>11</sup>

The foregoing technics as well as the details of postoperative care employed in our institutions have been described<sup>10,12</sup> but will be briefly commented upon as they relate to the problems now under discussion. Immunosuppressive agents were administered a day or more before transplantation. The stringency of the immunosuppression necessary to prevent homograft rejection was almost invariably greatest during the first few postoperative weeks or months. Success depended upon the manipulation of drug combinations which always included azathioprine (Imuran®). Prednisone was also usually given, often in very high doses. All patients who received corticosteroids were on a regimen of frequent ingestion of alkali and milk. Despite this precaution, there was a high incidence of complications of peptic ulcer<sup>10</sup>; this report deals only with those who were or should have been operated upon. Later patients in

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Submitted for publication March 1, 1968.

Supported by United States Public Health Service grants AM-06344, HE-07735, AM-07772, AI-04152, FR-00051, FR-00069, F05-TW-1154, AI-08898 and AM-12148.

the series were given adjuvant antilymphocyte globulin.<sup>12</sup> Threatened rejection of the homograft was treated by increasing the dose of prednisone, by local radiotherapy to the homograft and by the administration of actinomycin C.

In most patients who lived beyond the first few postoperative months, it was eventually possible to reduce the intensity of immunosuppressive therapy. The greatest adjustments were with prednisone.

### Results

There were 28 patients who developed one or more major intra-abdominal complications. These were divided into those diagnosed before, during, and after transplantation.

#### Pretransplantation

There were six complications in five patients. The most common was gastrointestinal bleeding due to peptic ulcer or gastritis (Table 1). The necessary gastric procedures proved to be neither dangerous nor difficult probably because the uremic state had been well controlled by several weeks of intermittent hemodialysis, and because the patients had ceased bleeding at the time of operation. Postoperative convalescence was rapid. Two months later, one

patient developed intestinal obstruction which was probably related to the original gastric procedure.

The patient in whom gastric perforation was caused by a peritoneal dialysis trocar was operated upon within 4 hours. After closure of the rent in the stomach, bilateral nephrectomy and splenectomy were carried out. She received a renal homograft 25 days later.

All five patients recovered promptly and later received renal homotransplantation; four are still alive from 9 months to 4½ years later. The only patient who subsequently died was one who required four operations pre- or post-transplantation for either gastrointestinal hemorrhage or intestinal obstruction (Tables 1 and 3). Death was eventually caused by hepatitis.

#### At Transplantation

Of five intra-abdominal complications at the time of bilateral nephrectomy, splenectomy, and renal homotransplantation (Table 2), none adversely affected the courses after transplantation. The five recipients are still alive 7 to 40 months after subsequent transplantation.

Only the intestinal obstruction was known in advance to be present. In this case, extensive lysis of adhesions was necessary.

TABLE 1. Six Problems in Five Patients Which led to Surgical Intervention in the Pretransplantation Period\*

Abdominal Problem	No.	Treatment	Recovered From Complication
Bleeding peptic ulcer or gastritis	4**	Vagotomy and drainage or partial gastric resection	4
Intestinal obstruction due to adhesions	1**	Lysis of adhesions	1
Perforation of stomach during peritoneal dialysis	1	Repair of gastric perforation	1

\* Homotransplantation was done from 13 to 88 days later. Four of the five recipients are still alive from 9 months to 4½ years after the homografting.

\*\* One patient had a partial gastrectomy and adhesiolysis 81 and 23 days, respectively, prior to transplantation. After transplantation, he required two more operations, one a vagotomy for recurrent GI bleeding and the other an adhesiolysis for a second intestinal obstruction (Table 3). He died of hepatitis 5 months after transplantation.

TABLE 2. *Problems Encountered and Treated in Five Patients at the Time of Transplantation\**

Abdominal Problem	No.	Treatment	Recovered From Complication
Right subhepatic abscess	2	Drainage	2
Intestinal obstruction due to adhesions	1**	Lysis of adhesions	1
Rectus sheath hematoma	1	Evacuation of hematoma	1
Pancreatic abscess	1	Removal of necrotic debris	1

\* These five recipients are all still alive after 7 to 40 months.

\*\* Nineteen and 55 days after homotransplantation this patient required two more operations, the first for a perforated gastric ulcer and the second for a closed loop intestinal obstruction (Table 3).

The sterile hematoma of the rectus sheath, resulting from laceration of the inferior epigastric artery, was a complication of peritoneal dialysis.

Two subphrenic abscesses were also thought to have resulted from previous peritoneal dialyses. The pancreatic abscess was in a patient who had a bout of acute pancreatitis almost one year earlier. In none of the three cases were organisms cultured from the collection of pus. Debridement and drainage were carried out.

#### Post-transplantation

**Early.** Eighteen of the 24 complications occurred within the first four post-transplantation months. Acute intestinal obstruction was the most common early problem and in every case it was possible to indict a specific etiologic factor. For example, two children who received transperitoneal homotransplantation had obstructing adhesions where the cecum and ascending colon were reflected to create a bed for the homograft. Two other patients were among those who had previously had intestinal obstructions treated before or at the time of transplantation. A foreign body left at an earlier operation was responsible in a fifth case and, in another, the bowel was trapped by an adhesive band near the incision used for nephrectomy and splenectomy. After relief of the obstruction all six patients recovered but two died at a later time from other causes.

During the first 4 months when steroid therapy was being given in high doses, there were four examples of perforation of a hollow viscus and four of gastrointestinal hemorrhage. Only one perforation was closed promptly; that patient, who had a gastric ulcer, survived. In another patient perforation of a sigmoid diverticulitis occurred more than 4 years after a first transplantation from a living nonrelated donor, and about 2 weeks after retransplantation with a cadaveric homograft. The eventual death of the patient was probably due to the fact that the diagnosis was not made and treatment was not instituted for another 2 weeks. In two other patients perforation from jejunal necrosis or gastric ulcer was not diagnosed until autopsy.

Three of four patients who had gastrointestinal hemorrhages in the early post-transplantation periods had uneventful recoveries. However, massive blood transfusions were required and two of the three patients died some months later from fulminating hepatitis. In one, a pretransplantation gastrectomy had been carried out and reoperation consisted of vagotomy and suture of the ulcer bed. The fourth patient, who had hemorrhagic gastritis at the time of vagotomy and pyloroplasty, died 6 days later of hemorrhagic enterocolitis.

Two distal pancreatic injuries apparently occurred at the time of splenectomy and left nephrectomy. In one a resulting pseudocyst was first drained and later excised

TABLE 3. *Twenty-four Intra-abdominal Complications Seen in 21 Patients from Two Days to More than Four Years after Renal Homotransplantation*

Abdominal Problem	No.	Treatment	Recovered From Complication
Intestinal Obstruction			
(a) Adhesions	6	(a) Lysis of adhesions	6
(b) Stricture of terminal ileum	1	(b) Resection of stricture	1
G. I. Bleeding			
(a) Duodenal ulcer	3	(a) Suture of ulcer; vagotomy and pyloroplasty	2
(b) Gastritis	3	(b) Vagotomy and pyloroplasty or hemigastrectomy	1
Appendicitis	2	Appendectomy	2
Pancreatic Lesions			
(a) Retroperitoneal abscess	1	(a) Multiple drainage procedures	1
(b) Pseudocyst	1	(b) Drainage; distal pancreatectomy	0
Perforated Diverticulitis with paracolic abscess	1	Transverse colostomy and drainage	0
Suspected Duodenal Perforation	1	Laparotomy	0
Perforated Gastric Ulcer	1	(a) Suture of perforation	1
	1	(b) None**	0
Retroperitoneal Abscess	1	None**	0
Jejunal Necrosis	1	None**	0
Hemorrhage from Splenic Artery	1	None**	0

\* Although 11 patients convalesced satisfactorily from one or more complications, three of these died three, three, and 15 months after their last laparotomy from generalized bacterial sepsis, hepatitis, and hepatitis respectively.

\*\* These lethal complications were found at autopsy.

in continuity with the pancreatic tail. Reoperation was necessary for secondary hemorrhage and the patient eventually died of septicemia. In the other patient, a widely dissecting retroperitoneal abscess was drained on several occasions during the third and fourth post-transplantation months. After a very stormy course the patient recovered. The case has been reported in detail<sup>12</sup> since the crucial factor in recovery seemed to be the ability to drastically reduce steroid therapy. This was made possible by the addition of heterologous antilymphocyte globulin to a pre-existing immunosuppressive regimen.

A fatal intra-abdominal hemorrhage from the splenic artery caused the death of a

patient 2 days after splenectomy. In a final case, abdominal exploration was carried out for the diagnosis of perforated duodenal ulcer. No intra-abdominal abnormalities were found.

**Late.** Six complications occurred after 4 months. Three patients were operated upon from 14 to 31 months after transplantation at a time when their immunosuppressive therapy had been lightened, and when they had essentially normal renal function. Two had appendicitis, and in one the diagnosis was obscured for a few hours because of the proximity of the appendix to a right lower abdominal graft. The third patient was a child who earlier required lysis of adhesions for intestinal obstruction.

Two and a half years later she developed an ileal stricture which was resected. In all three cases recovery was uneventful.

Each of the other three patients had reduced but life sustaining renal function. One with upper gastrointestinal hemorrhage due to duodenal ulcer received a pyloroplasty and vagotomy 6 months post-transplantation and died a few weeks later. He had multiple fungal and bacterial brain abscesses which had evidently been present for many months. A second patient who died one week after vagotomy and hemigastrectomy for massive bleeding from severe gastritis, was 2½ years post-transplantation. At autopsy reticulum cell sarcoma was found in the liver, lung, pituitary gland, thyroid, prostate, skeletal muscle and skin. The third patient was well for more than a year after receiving a homograft. He then developed severe hepatitis followed by septicemia. At autopsy, the same bacteria which had been found in the blood stream were isolated from a large abscess in the left renal fossa. Removal of a large polycystic kidney 13 months previously had been unusually difficult.

#### Discussion

There are a number of factors which probably contributed to the high incidence of intra-abdominal complications and to the difficulties of diagnosis and treatment. At some time or other, the abdominal cavity of virtually every patient was entered. In some this was for peritoneal dialysis; in others, particularly children, for intra-abdominal placement of the homografts; and in almost all for nephrectomies and splenectomy. Each of these interventions was the direct cause of some subsequent morbidity.

Of far greater importance, however, were metabolic factors introduced first by the variable degrees of uremia and by the immunosuppressive agents used to prevent rejection of the homografts. Uremia is a notorious cause of a variety of gastrointestinal

disorders including pain, gastrointestinal bleeding, pancreatitis, enterocolitis, and ileus.<sup>2, 8, 9, 13</sup> In addition, the immunologic reactivity of the patient with renal failure is often reduced<sup>3, 6</sup> so that he can less effectively deal with intraperitoneal sepsis.

After transplantation, the use of immunosuppressive drugs can lead to further immunologic crippling, particularly if the homograft does not cause prompt and continuous resolution of the renal failure. Apart from rendering the recipient more susceptible to infection there are other specific disadvantages to the use of these agents. Since azathioprine is a potential bone marrow depressant, it can prevent a diagnostic leukocyte rise in response to a septic complication if overdoses are inadvertently given. Antilymphocyte globulin can confuse the diagnosis by causing fever.

However, the chief source of diagnostic confusion, morbidity, and mortality has proved to be prednisone. It is known that adrenal cortical steroids can cause gastrointestinal ulceration and bleeding,<sup>7, 10</sup> pancreatitis,<sup>1, 4, 10</sup> suppression of the febrile response and masking of the diagnostic physical findings of peritonitis.<sup>5</sup>

Inasmuch as renal function tends to be unstable for several weeks after homotransplantation and the need for immunosuppression is usually greatest at this time, it is not surprising that the preponderance of intra-abdominal complications, misdiagnoses, and fatalities occurred during the first 4 postoperative months. In many unsuccessfully treated patients the relative contributions of prednisone therapy and subnormal renal function were impossible to assess. Even during this dangerous interval, however, the best chance for survival was when a complication was immediately diagnosed and promptly treated. If these objectives were not met the immediate or delayed mortality was excessive. If surgical therapy were carried out either before this time of predictably high risk or long afterwards when homograft function was stable with

reduced doses of the immunosuppressive drugs, convalescence was often indistinguishable from that expected in a normal person.

In view of retarded healing which has been said to result from immunosuppressive therapy, it is of interest that no serious wound complications were encountered in any of these patients despite the multiple reopening of some of the incisions. Extraordinary precautions were taken in the operating room to maintain strict asepsis. However, the most important details of care were probably meticulous hemostasis and careful technics of wound repair. Within the peritoneal cavity and at all stages of closure, copious irrigations were used and antibiotic agents were instilled locally. Fine nonabsorbable suture material was almost always employed even in the presence of potential contamination. Stay sutures were avoided. During and after operation, carefully selected antibiotic agents were given parenterally.

### Summary

One or more major abdominal complications developed in 28 of 184 patients either before or after renal homotransplantation. These complications included gastrointestinal hemorrhage, intestinal obstruction, perforation of a hollow viscus, abscesses, appendicitis, hemorrhage, and pancreatic pseudocyst in that order of frequency. Factors which contributed to this high incidence of intra-abdominal disease included the variable presence of uremia, and the use in the post-transplantation period of immunosuppressive agents, particularly adrenal corticosteroids.

With prompt and aggressive surgical therapy, there was a high rate of recovery from these surgical emergencies although a number of the successfully treated pa-

tients subsequently died from other causes. Four lethal complications were not diagnosed until the time of autopsy. Fifteen of the 28 patients are still alive 3 months to 4½ years after homotransplantation.

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