

## EFFECT OF LOCAL IRRADIATION ON THE ACUTE REJECTION PROCESS IN TRANSPLANTED KIDNEYS

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Acute rejection occurs in the non-sensitized host in response to a foreign graft. It is believed to be caused by sensitized lymphocytes and plasma cells. In the homo-transplanted kidney, these cells injure small blood vessels leading to ischemia and loss of function (KOUNTZ et coll. 1963).

The radiation sensitivity of lymphoid cells is well documented: 150 R cause a pycnotic degeneration of 50 per cent of the lymph node cells in vivo in the rat (TROWELL 1952). Irradiation has been demonstrated to reverse a rising blood urea nitrogen during acute rejection episodes in dogs (KAUFFMAN et coll. 1965). From these facts it may be postulated that irradiation may transiently reverse an acute rejection phenomenon by destroying the lymphocytes at the site of injury. In human renal transplantation, irradiation is used to acutely arrest the rejection process, allowing other methods of treatment. The purpose of this report is to review the effectiveness of this treatment.

### Material and Methods

Between January 1968 and December 1974, 178 renal transplant patients received local irradiation of their graft in an effort to halt acute rejection phenomena. The mean age was 27 (range 9 to 54). The transplant was taken from either a sibling, parent or child in 108 patients (61 %); 70 (38 %) received cadaveric kidneys. All

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Supported in part by the Washington Division, Inc., American Cancer Society, Summer Student Fellowship Program, and Public Health Service Grants CA-12441, CA-05198 and Ca-12260 from the National Cancer Institute. Submitted for publication 31 January 1977.

*Acta Radiologica Therapy Physics Biology* 16 (1977) Fasc. 3 June

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**Table**

*Number of transplants functioning 6 months, 12 months, and 18 months after irradiation for acute rejection. Percentage given in parentheses*

| Functioning at     | 6 months | 12 months | 18 months |
|--------------------|----------|-----------|-----------|
| Total 178          | 119 (67) | 101 (58)  | 88 (49)   |
| Cadaveric donor 70 | 41 (59)  | 34 (48)   | 24 (34)   |
| Related donor 108  | 78 (72)  | 69 (64)   | 64 (59)   |

patients received 3 irradiations with 1.5 Gy (150 rad) on alternate days (4.5 Gy total) once the diagnosis of acute rejection was made. The patients were irradiated with megavoltage equipment through a single anterior port. Ten patients received a second course of irradiation.

Pretransplant treatment consisted of high dose steroids, azothioprime, and anti-lymphocyte globulin, and during a rejection process the patient received additional steroids as well as irradiation. This phase of the treatment has been reported elsewhere (MARCHIORO & TREMANN 1974). If necessary, the patient was dialyzed during the acute phase.

The diagnosis of acute rejection was established by the following clinical and biochemical indicators: fever, graft tenderness, decreased blood flow through the graft, decreased urine output, increased blood urea nitrogen, and increased serum creatinine.

The date of permanent rejection was taken to be the time of return to dialysis or removal of the transplant, whichever occurred first. All patients have been followed for 18 months. Eleven patients have been lost and were presumed to have failed at the date of last follow-up.

### Results

Of 178 transplanted kidneys with acute rejection, 59 (33 %) failed within 6 months of irradiation. A total of 75 (42 %) failed before 12 months, and 90 (51 %) failed before 18 months (Table).

For 108 patients receiving kidneys from related donors, 30 (28 %) failed before 6 months, 39 (36 %) failed before 12 months, and 44 (41 %) had failed by 18 months. For the 70 recipients of cadaveric kidneys, 29 (41 %) failed within 6 months, 36 (52 %) by 12 months, and 46 (66 %) by 18 months. Both groups had most of their failures during the first 6 months following irradiation.

### Discussion

Irradiation of the graft site before transplantation has been tried in an effort to destroy local lymphatic tissue; this does not improve the longevity of a transplanted

kidney (WOODRUFF et coll. 1963). Irradiation of the donor kidney before transplantation in an effort to alter its antigenicity likewise has not been successful (HUME et coll. 1960). Irradiation is most effective when used for the destruction of sensitized lymphocytes in the acutely rejecting graft, thus blocking the active arm of the immune response.

Clinical experience with irradiation used in this manner has been variable. In one series, 70 per cent of humans with acute rejection and a blood urea nitrogen of 75 mg % or more obtained a reduction by at least 20 per cent of its preirradiation value (ABRAMSON et coll. 1974). The oliguric patients also increased the urine output. Another group reported a decreased graft and patient survival at one year when 6 Gy and steroid therapy was compared to controls receiving only steroids (26 % versus 50 %) (GODFREY & SALAMAN 1976). In the present series, 58 per cent of the grafts were functioning one year after transplantation (64 % with related donors). These results are considered to justify the continuing use of irradiation as part of the treatment for acute rejection of a transplanted kidney.

### SUMMARY

The graft in 178 renal transplant patients was irradiated in an effort to halt acute rejection phenomena. Of the patients, 61 per cent received their transplant from either a sibling, parent or child and 38 per cent received cadaveric kidneys. Of the irradiated kidneys 61 per cent were functioning at 6 months, 58 per cent at 12 months and 49 per cent at 18 months. The rationale for irradiation of transplanted kidneys with acute rejection is discussed.

### ZUSAMMENFASSUNG

Um akute Abstossphänomene aufzuhalten, wurde das Nierentransplantat von 178 Patienten bestrahlt. Von den Patienten hatten 61 Prozent ihr Transplantat entweder von Geschwistern, Eltern oder einem Kind erhalten und 38 Prozent erhielten Kadavernieren. Von den bestrahlten Nieren waren 61 Prozent nach 6 Monaten, 58 Prozent nach 12 Monaten und 49 Prozent nach 18 Monaten funktionsfähig. Die besonderen Gründe für die Bestrahlung der transplantierten Niere bei akuter Abstossung werden diskutiert.

### RÉSUMÉ

Chez 178 sujets ayant subi une transplantation rénale, la greffe a été irradiée pour essayer d'éviter le phénomène de rejet aigu. Parmi ces sujets, 61 pour-cent ont reçu leur transplant d'un frère ou sœur ou d'un parent ou d'un enfant et 38 pour-cent ont reçu les reins de cadavres. Sur les reins irradiés, 61 pour-cent fonctionnaient au bout de 6 mois, 58 pour-cent au bout de 12 mois et 49 pour-cent au bout de 18 mois. Les auteurs discutent la justification de l'irradiation de reins transplantés atteints de rejet aigu.

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