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Infectious Complications Associated with Renal Transplantation: An Analysis of Risk Factors

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To assess the multiple risk factors reported to be associated with onset of serious bacterial, fungal, viral, and protozoal infections in renal allograft recipients, a retrospective study of all renal transplantations performed at Yale-New Haven Medical Center from the inception of the transplantation program in December, 1967, to December, 1975, was undertaken.

Ninety-six renal allograft transplants in 85 patients were available for evaluation during this study period. Renal allograft recipients were evaluated for incidence of infection from time of transplantation until transplant nephrectomy, death, or January 1, 1976. All infections were characterized by type of infection, organism, site, and time of onset post-transplantation. Recipients with infections were also evaluated for their donor type, living-related or cadaveric, age at time of transplantation, granulocytopenia, corticosteroid therapy, and rejection episodes.

There were 215 infections, 92 of which were defined as serious, in 78 of the 96 renal allograft recipients. Eighteen renal allograft recipients had no infections. Granulocytopenia, but not rejection, correlated with serious infections at some time in the patient's course. However, no significant *temporal* relationship between serious infections and episodes of granulocytopenia or rejection could be established. Mortality rate and incidence of serious infection was higher in the group receiving high dose corticosteroid therapy compared with the group receiving lower doses of corticosteroids. The mortality rate in these 85 transplant recipients was 33%. Seventy-four percent of these deaths were directly related to infection (24% of 85 patients).

INTRODUCTION

Serious bacterial, fungal, viral, and protozoan infections comprise the well-documented causes of morbidity and mortality in the immunosuppressed patient population [1-3]. Risk factors which predispose renal allograft recipients to their infections have been suggested, but no unifying hypothesis has been established [4-9]. The present study, therefore, was undertaken to assess multiple risk factors through a retrospective evaluation of all renal transplantations performed at Yale-New Haven Medical Center from the inception of the program in December, 1967, until December, 1975. In particular, potential *temporal* relationships between episodes of granulocytopenia, allograft rejection, and infection were evaluated.

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MATERIALS AND METHODS

Population

One hundred and forty-eight renal allograft transplantations were performed in 135 patients at Yale–New Haven Medical Center between December, 1967, and December, 1975. Thirty of the 148 renal transplants were performed on 29 patients in the West Haven Veterans Administration Hospital and were not evaluated in the present study. Also, the infectious complications in 21 patients with 22 of the remaining 118 renal allografts could not be properly evaluated since documentation of particular findings needed for the diagnosis of the infection (see definitions) was not available in the hospital record or the post-transplant flow sheet. Therefore, 96 renal allografts performed in 85 patients were available for evaluation and comprise the patient population of this retrospective study. All charts were evaluated from the time of transplantation until removal of the transplanted kidney, death, or January 1, 1976, whichever occurred first.

Retrieval of Data

All data was retrieved according to the methods described by Feinstein for retrospective chart analysis [10,11]. Thus, cases were excluded from analyses of incidences of particular findings if the presence or absence of these findings were not clearly documented. Therefore, the data presented represent the number of cases of renal allograft recipients with positive findings in relationship to the number of cases when verifications of positive or negative findings could be made.

The data on each transplant recipient were obtained from two sources: the hospital record and the immediate post-transplant flow sheets maintained by the renal section. The following data were obtained for all patients: sex, age, and weight at time of transplant, race, type of renal disease, donor type (cadaver or living related), and date of transplant operation. In addition, white blood cell count with percent polymorphonuclear leucocytes, blood urea nitrogen, creatinine, dosages of corticosteroids, azothioprine, actinomycin D, and anti-lymphocytic globulin (ALG), as well as all diagnostic procedures including microbiology studies, chest roentgenograms, renal scans, and biopsies were also evaluated.

All infectious complications which occurred during each post-transplant hospitalization were documented as to etiology, site, and clinical course. Infections were classified by the following criteria:

Symptomatic urinary tract infection. A single clean catch or catheter urine specimen containing greater than 100,000 colonies per milliliter bacteria, in association with clinical signs of infection which included fever, dysuria, urgency, and frequency.

Lower respiratory tract infection. Patients with any four of the following six criteria were classified as having lower respiratory tract infection: (1) temperature $>99.4°$F orally or 100°F rectally; (2) cough, purulent sputum; (3) chest roentgenogram demonstrating alveolar or interstitial infiltrates that did not clear with vigorous diuresis or dialysis; (4) a clinical history not compatible with pulmonary embolization; (5) isolation of a single or predominant pathogenic organism(s) from a tracheal aspirate or pulmonary biopsy specimen; or (6) isolation of the same organism from cultures of blood and sputum in close temporal proximity.

Septicemia. Septicemia was diagnosed if the identical organism(s) was present in two or more blood culture sets obtained at separate time intervals.

Surgical-abdominal wound infection. Any surgical wound with purulent drainage with or without a positive culture was considered infected. Positive cultural findings in serous drainage was considered an infection if accompanied by tenderness and fever with no other apparent source of infection. This was classified as a urinary cutaneous fistula infection if the drainage fluid was urine. Arteriovenous fistulas were considered a surgical infection.

Peritonitis. The diagnosis of peritonitis was made with or without positive cultures if there were positive abdominal findings on physical exam *and* more than 300 polymorphonuclear leucocytes in the peritoneal fluid.

Perinephric abscess. A perinephric abscess was documented by findings at surgical exploration and/or by abdominal arteriography.

Hepatitis. Hepatitis was diagnosed in any patient with abnormal liver function studies and compatible physical findings. A positive hepatitis B surface antigen was not necessary for the diagnosis.

Meningitis. Patients with fungal or bacterial organisms isolated from cerebrospinal fluid cultures or with cerebrospinal fluid pleocytosis and fever were classified as having meningitis.

Pericarditis. Pericarditis was diagnosed by the presence of a pericardial friction rub and the recovery of microorganisms from culture of pericardial fluid.

Endocarditis. Patients with one or more of the following criteria were classified as having endocarditis: endocarditis at autopsy; a pathologic murmur, i.e., a murmur in diastole, a new or changing murmur, and/or sustained bacteremia, defined as four or more blood cultures positive during a period of evaluation for sepsis without an apparent, alternative site of intravascular infection.

Skin infection. Patients with purulent drainage or a positive culture obtained from the involved area plus any two of the following criteria: heat, redness, swelling, or tenderness, were classified as having an infection of the skin. Skin infections were sub-divided into four groups: superficial skin infections including cellulitis and IV site infection, *Herpes simplex*, *Herpes zoster*, and skin abscesses.

Unexplained fever. An unexplained fever was defined by a temperature >99.4°F orally or 100°F rectally without evidence of graft rejection and with no source or infecting agent identified within five days. Unexplained fever was not considered to be an infection in this analysis.

Asymptomatic bacteriuria. Asymptomatic bacteriuria was defined as two or more clean catch or catheterized urine specimens containing >100,000 colonies per milliliter of a single species of bacteria for females and >10,000 colonies per milliliter of a single species of bacteria for males without clinical symptoms. Asymptomatic bacteriuria was not considered an infection in this analysis.

Serious infections. Pneumonia, meningitis, peritonitis, pericarditis, endocarditis, septicemia, perinephric abscess, disseminated varicella and nocardia, suppurative parotitis, and all urinary tract or wound infections associated with a concomitant bacteremia with the same organism were considered serious infections.

Risk Factors Evaluated

Rejection episodes. An acute rejection episode was defined by the criteria used by the renal section at this institution and include a decrement in renal function, fever, tenderness at graft site, abnormalities in technetium 99 blood flow scan and renal biopsy. Only those instances in which no other cause could be found to explain the above abnormalities, and where immunosuppressive therapy was altered to treat rejection, were included in this analysis as rejection episodes.

Severe granulocytopenia. Severe granulocytopenia was defined as a polymorphonuclear leucocyte cell count equal to or less than 1000 cells/mm^3 blood on two sequential differential white blood cell counts.

Relative granulocytopenia. A polymorphonuclear leucocyte cell count greater than 1000 and less than or equal to 2000 cell/mm^3 blood on two sequential differential white blood cell counts was considered to be relative granulocytopenia.

Granulocytopenia. Granulocytopenia was defined as a polymorphonuclear leucocyte cell count of less than 2000 cells/mm.^{3} This included both severe and relative granulocytopenia.

Corticosteroid therapy. High dose corticosteroid therapy was defined as a steroid dose equivalent to one or more milligrams per kilogram per day of prednisone for 27 of the first 60 days after transplantation. This definition was chosen since, as noted by Finkelstein and Black [7] in their analysis of a segment of this population, one episode of acute rejection, to which the patient responded successfully, usually involved high dose (1 mg/kg prednisone) corticosteroid therapy for 26 or fewer days within the first 60 days.

Age and allograft. Patients' age at time of transplantation, and type of allograft, i.e., cadaver, or living-related, were also correlated with incidence of infection.

Data Analysis

The incidence of infection was based on the observation of the number of times a particular infection occurred divided by the total number of renal allograft recipients (96 renal allografts). Mortality data is calculated from the total number of patients in the analysis (85 patients). Statistical significance was determined by chi square analysis using Yates correction factor for small numbers [12].

RESULTS

Population

In this study population, 96 renal allografts were performed in 85 patients, eleven of whom received two renal allografts. There were 21 living-related donors and 75 cadaveric donors. Patients ranged in age between one and 56 years. There were 51 males and 34 females. Eight males and three females received two renal allografts. The population included 61 Caucasians, 20 Blacks, two Hispanic and two Asian patients.

Primary renal diseases included 31 patients with chronic glomerulonephritis, 7 patients with malignant hypertension, 5 patients with chronic pyelonephritis, 5 patients with interstitial nephritis, and 2 patients each with systemic lupus erythematosis, diabetic nephropathy, Wegener's granulomatosis, obstructive uropathy, and hereditary medullary cystic disease. Single cases of uric acid nephrocalcinosis, rapidly progressive glomerulonephritis, renal cell carcinoma, and congenital multicystic disease were also reported. In 20 patients, the primary renal disease was not known.

Infections

Two hundred and fifteen infections were documented in 78 of the 96 renal allografts. Of the 215 infections, 92 were considered to be serious as previously defined. These occurred in 45 of the 78 allografts who had some type of infection, whereas 33 of these 78 recipients had non-serious infections and 18 renal allograft recipients (17 patients) had no infection throughout their course. Figure 1 demonstrates that in every age group there was a higher percentage of serious infections in

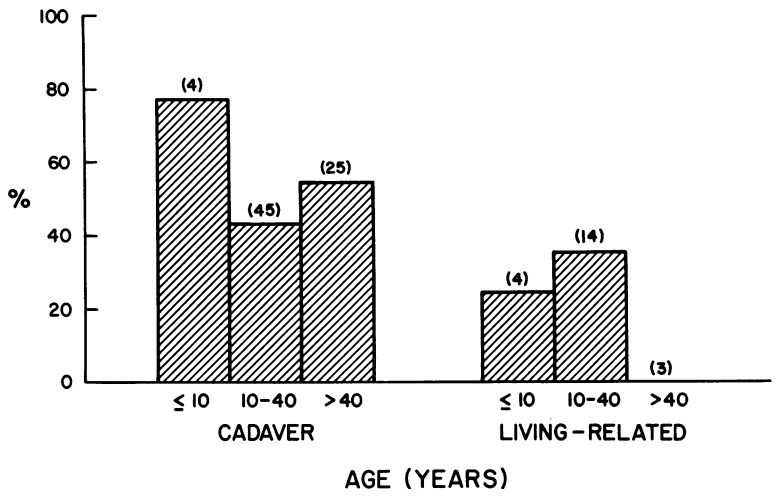

FIG. 1. Percent of allograft recipients with serious infections compared to donor type and age of recipient at transplantation. (Figure in parenthesis represent the number of allograft recipients in each group).

patients with cadaveric donors. In addition, patients with cadaveric kidneys under the age of 10 and over 40 had a greater percentage of infections compared with cadaveric recipients between the ages of 10 and 40. Although this finding is not statistically significant ($0.1 < p < 0.2$), the numbers of patients less than 10 years and greater than 40 years of age were small. The urinary tract was the most common site of infection in our population of renal allograft recipients. However, among the serious infections, septicemia and lower respiratory tract infection were most frequent, with 34 respiratory tract infections and 28 episodes of septicemia documented. Other serious infections included hepatitis in 4 patients, meningitis in 3 patients and pericarditis and endocarditis in one patient each (Table 1). There were five episodes of unexplained fever and 7 of asymptomatic bacteriuria.

The etiology of these infections is shown in Table 2. Bacterial organisms were the major pathogens and caused approximately 80 percent of infections in renal allograft recipients. Viral and fungal organisms each caused approximately six percent of infections. Mixed bacterial and fungal agents accounted for three percent of the infections. In five percent no causative agent could be found.

Infectious organisms cultured from the urinary and respiratory tracts, blood, surgical abdominal wound, urinary cutaneous fistula, perinephric abscess, and central nervous system are shown in Fig. 2. Most urinary tract infections were caused by gram-negative bacilli, predominantly *E. coli.* Bacteria were responsible for 23 of 31 lower respiratory tract infections. In addition, two patients developed *pneumocystic carinii* pneumonia. Single cases of aspergillosis, nocardiosis, and an unknown yeast were observed. *Listeria monocytogenes* and *Staphylococcus aureus* were the most common organisms isolated from blood and were each responsible for 20 percent of bacteremic episodes. The six episodes of *Listeria monocytogenes* sepsis occurred within a 12-month time period in this hospital. An extensive epidemiologic evaluation revealed no common source, although four of the six clinical infections were of the same subgroups. Sixty-seven percent of abdominal wound infections were caused by mixed gram-negative and gram-positive bacteria, and thirty percent were of staphylococcal origin. All urinary cutaneous fistula infections were of mixed

TABLE 1
Types of Infections in 96 Renal Allografts at Y-NHH
December 1967–December 1975

Site	No. Episodes	No. Allografts	Percent*
Urinary tract	62	38	40
Respiratory tract			
Upper	3	3	
Lower	31	23	
Total	34	25**	26
Septicemia	28	21	22
Surgical-abdominal wound	24	23	24
Skin			
Herpes zoster	2	2	
Superficial	5	4	
Herpes simplex	6	6	
Abscess	11	9	
Total	24	19**	19
Intra-abdominal			
Perinephric abscess	5	5	
Peritonitis	6	6	
Total	11	11	12
Urinary cutaneous fistula	8	8	8
Other wounds			
Femoral, hip, thoracotomy	4	4	
C-section, wrist, fistula	4	4	
Total	8	8	8
Hepatitis	4	4	4
Gastrointestinal			
Esophagitis	1	1	
Proctitis	1	1	
Suppurative parotitis	2	2	
Total	4	4	4
CNS-meningitis	3	3	3
Cardiac			
Pericarditis	1	1	
Endocarditis	1	1	
Total	2	2	2
Other			
Disseminated varicella	1	1	
Disseminated nocardia	1	1	
Total	2	2	2
ENT—Maxillary sinusitis	1	1	1
Unexplained fever†	5	5	5
Asymptomatic bacteriuria†	7	7	7

*Number of allografts with this infection/total number of allografts

**Allograft recipient had infection in more than one category contained under this heading

†Not considered on analysis as infections

TABLE 2
Etiologic Agents Causing Infections in 96 Renal Allograft Recipients

Site of Infection	Total No.	Etiology (No.)					
		Bact.	Fungal	Viral	P. Carinii	Bact. Fung.	Unknown
Urinary tract	61	62					
Respiratory	34	20	3	3	2	3	3
Septicemia	28	26	2				
Surg-abdominal wound	24	24					
Skin	24	12	3	8			1
Urinary cutaneous fistula	8	8					
Other wounds	8	7				1	
Peritonitis	6	5				1	
Perinephric abscess	5	5					
Hepatitis	4*			2			2
Meningitis	3	1	1				1
Suppurative parotisis	2	1					1
Pericarditis	1	1					1
Endocarditis	1						
Disseminated							
varicella	1			1			
nocardia	2		1				
Esophagitis	1		1				
Proctitis	1		1				
Maxillary sinusitis	1	1					
TOTALS	215	173	12	12	2		11

*Two patients were hepatitis B surface antigen positive, one was negative, and one was not tested. Cytomegalovirus and toxoplasma titers were not available for any of the four recipients with hepatitis.

bacterial origin composed of gram-negative bacilli and *Staphylococcus aureus.* Infections in this patient population were analyzed relative to rejection episodes, granulocytopenia, and high dose steroids.

Infections–Rejections

The time of all documented infections and rejections in the post-transplant period is shown in Fig. 3. The highest incidence of both infections and rejections occurred within the first sixty days after transplantation. However, after the first post-transplantation year transplant rejection became a relatively minor contribution to morbidity, whereas late onset infection persisted and was a major factor in the morbidity and mortality, i.e., 48% of the surviving recipients in this study experienced a documented infection after one year while only 7% had a rejection episode.

Two of the 96 recipients experienced a severe rejection episode within the first 72 hours and underwent transplant nephrectomies. In the remaining 94 recipients the number of serious infections were compared between 73 recipients with two or less rejection episodes and 21 recipients with three or more rejection episodes during their clinical course. Twenty-nine of the 73 recipients with two or fewer rejection episodes had 65 serious infections (2.2 infections per patient) while 12 of 21 recipients with three or more rejection episodes had 31 serious infections (2.6 infections per patient). The differences between the two groups was not statistically significant ($p \geq 0.20$).

Infection–granulocytopenia. Seven of the 94 evaluable recipients had episodes of severe granulocytopenia (granulocytes $\leq 1000/mm^3$) and 13 recipients had an

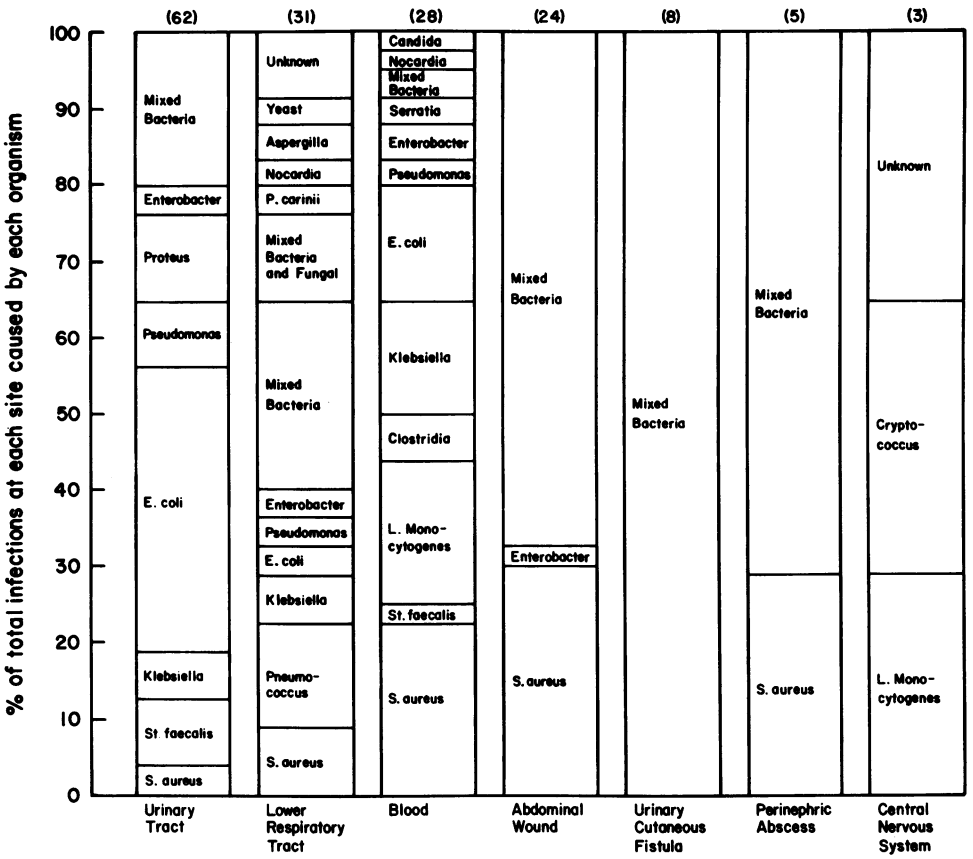

FIG. 2. The infectious agents causing infection at different sites in the 78 renal allograft recipients who developed infection. Within each site the percent of infections caused by each organism is roughly calculated. Microorganisms causing infection at additional sites listed in Table 2 are not included in this figure thus the total number of infections does not equal 215. Number in parenthesis indicate the actual number of infections in the 78 renal allograft recipients at each site.

episode of relative granulocytopenia (granulocytes $\geq 1000 \leq 2000/mm^3$) (Fig. 4). Nineteen of the 20 granulocytopenia recipients had received cadaveric allografts. Of the seven recipients with severe granulocytopenia, 5 (71.4%) had a total of 15 serious infections. Ten of the 13 patients (77%) with relative granulocytopenia experienced 28 serious infections post-transplantation. Twenty-five (34%) of the 74 non-granulocytopenic recipients had 49 documented serious infections at some time in their evaluated course.

The incidence of serious infection in severe granulocytopenic recipients compared with the non-granulocytopenic group was not significant ($0.10 > p < 0.20$). This may be related to the small number of allograft recipients in the severe granulocytopenic group, since the incidence of serious infection in the relative granulocytopenic recipients compared with the non-granulocytopenic group was significant ($p \leq 0.01$), as was the incidence when both severe and relative granulocytopenic groups were combined and compared with the non-granulocytopenic group. There was no significant difference in the number of serious infections between the severe and relative granulocytopenic groups.

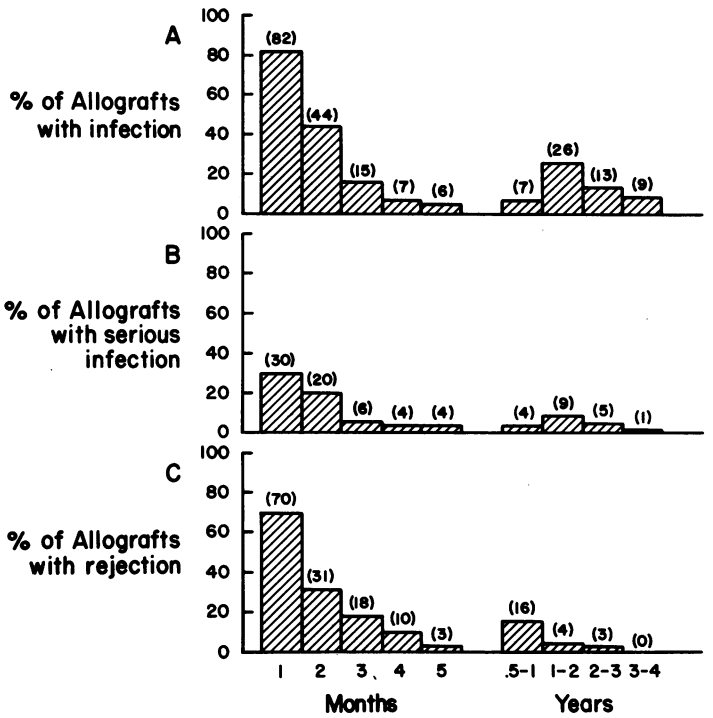

FIG. 3. Time of occurrence of all documented infections and rejections in the post transplantation period. Number in parenthesis equals the percentage of allograft recipients with the entity. Percentage equals number of allografts with the entity/total number of allografts evaluable for the entity.

To determine whether a temporal relationship existed between granulocytopenic and rejection episodes with infections, the separate incidences of granulocytopenias and rejections occurring for the five days preceding and the five days following the diagnosis of infection were compared. All infections in the early postoperative period and all serious infection throughout the clinical course were included in this analysis.

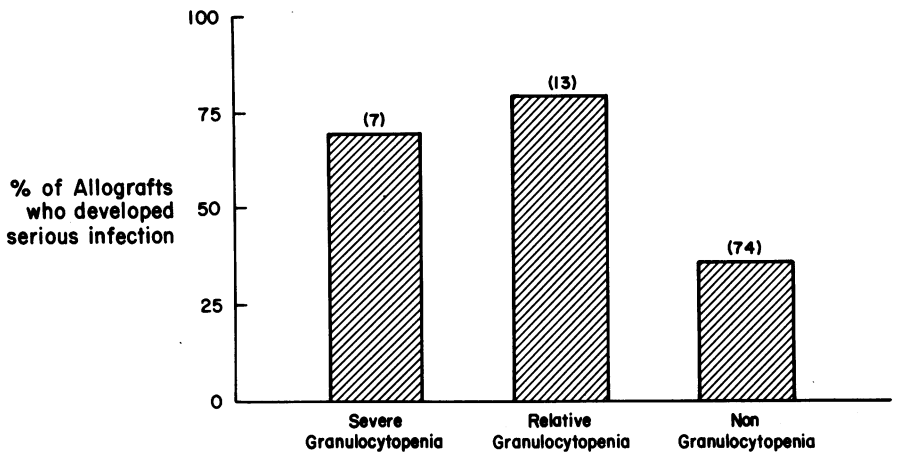

FIG. 4. Percentage of allograft recipients who developed serious infection relative to episodes of granulocytopenia at anytime post transplantation. Number in parenthesis is the total number of allografts in each group.

Twenty renal allograft recipients, of the 94 evaluated, had 32 episodes of granulocytopenia during their clinical course. Nineteen of these recipients had at least one episode of granulocytopenia during the early postoperative period. In this period 10 of the 19 recipients with granulocytopenia had 21 infections temporally associated with the granulocytopenia episode. Fifty-nine of the remaining 75 allograft recipients had 113 infections not temporally associated with a granulocytopenic episode in this period. This difference was statistically significant ($p = <0.05$) with a higher incidence of infections in those patients who were not granulocytopenic. Eight of 20 patients with granulocytopenia at some time in their course rather than just the early postoperative period had 15 *serious* infections temporally associated with granulocytopenia. The remaining 12 patients had no incidence of temporally related serious infection.

In evaluating the association between infections and rejection episodes, we found that 26 of the 94 allograft recipients studied had 42 infections in the five-day period preceding and/or following a rejection episode. Fifty-four renal allografts experienced 76 episodes of rejection without an associated infection. Fourteen recipients had no rejection episode during this period, and nine of these experienced infection.

Of the 96 allograft recipients initially in the study, 39 were evaluated for any association between serious infection and low or high dose corticosteroid therapy. The remaining 57 patients were excluded because of transplant nephrectomy, discharge from hospital prior to 60 days, or death. High dose therapy was administered to 21 of these 39 recipients while 18 received low dose steroids.

Serious infections occurred in 16 of the recipients on high dose therapy (75%) and 11 of the low dose steroid group (60%). Although the small number of patients receiving steroids precluded a statistical analysis of morbidity and mortality with the high and low dose groups, we noted that the mortality rate in the group on high dose steroid was 33%, but only 11% in the low dose group.

At the conclusion of the study period 82 of the 85 patients remained available for evaluation. The status of three was unknown. Twenty-nine of these patients exhibited stable renal function (creatinine < 2.5 mg%), 26 patients had returned to dialysis, and 27 patients died. Of the 27 deaths, 21 (74%) were attributable to infectious complications. Table 3 presents the sites and the organisms responsible for these fatal infections. Pneumonias accounted for the major cause of death either as single fatal events or as major parts of septic events. Gram-negative pathogens accounted for eight deaths either as single isolates causing pneumonia or as mixed flora in combined abdominal and respiratory tract infections. Of the opportunistic infections pneumocystis carinii, aspergilla species, and nocardia accounted for two deaths each while disseminated candidiasis was responsible for one death.

DISCUSSION

Finkelstein and co-workers at this institution have emphasized the need to explore further the role of predisposing risk factors to negative outcomes in renal transplants in view of high reported patient mortalities and graft failure rates [7]. The overall mortality rate in our series was 33% and approximately the mortality rate found by Anderson et al. [4] and Gurland et al. [14] though it is higher than a recently reported series from Belfast [13].

In an attempt to isolate specific potential risk factors in the present study each transplant recipient was evaluated according to stricter definitions of leukopenia and infection than have been employed in previous studies by others. Prolonged high

TABLE 3
Type of Infection and Organism(s) Leading to Death in 21 Renal Allograft Recipients

Type of Infection	POD*	Causative Organism(s)
Pneumonia	60	Pneumocystis carinii
Pneumonia	51	E. coli
Pneumonia	533	Aspergilla
Pneumonia	69	Staphylococcus aureus
Pneumonia	61	Pneumocystis
Pneumonia	103	Mixed gram-negative organisms
Pneumonia	192	E. coli
Pneumonia	138	Nocardia
Peritonitis	716	Mixed bowel flora
Peritonitis	73	Mixed bowel flora
Peritonitis	948	Mixed bowel flora
Peritonitis	118	Mixed bowel flora
Bacteremia	747	E. coli
Bacteremia	1066	Listeria monocytogenes
Perinephric abscess	35	Staphylococcus aureus
Perinephric abscess	24	Enterobacter
Bacteremia perinephric abscess	46	Candida
Disseminated zoster	185	Varicella
Disseminated nocardia	215	Nocardia
Fungemia	73	Aspergilla
Bacteremia Peritonitis	32	Mixed bowel flora

*POD: Postoperative day

dose corticosteroid therapy as a potential risk factor was similarly analyzed for a correlation with infection and mortality. The infections that occurred in our series of recipients were similar to those found in other studies [8,15,16]. In general the most common early postoperative infections were from the urinary tract and these represented 29% of the 215 infections in the series. What we defined as serious infections represented 42% of all infections (92/215). In this group there was a 30% incidence of sepsis and a 34% incidence of pneumonia. Thus, like Turcotte [16], we found pneumonia to be a common event associated with a high mortality rate. Gram-negative bacteria were the most common pathogens in these infections.

As others have reported, we found a correlation between granulocytopenia and serious infections. Anderson et al. [14], using a rather broader definition of leukopenia (total white blood cells of less than $3000/mm^3$ for a minimum of three consecutive determinations on different days) were unable to demonstrate a significant temporal association between episodes of infection and episodes of granulocytopenia. In a smaller study, Simmons et al., using an equally broad definition, observed 18 episodes of leukopenia in a group of 9 patients with a correlation noted in 13 infections [5]. A further restriction of this study, however, was a minimal survivor time of all 98 patients of at least 250 days from transplantation. With regard to evaluating leukopenia further as a risk factor we chose parameters that took into account Bodey's and his co-workers correlation between increased incidence of infection and granulocyte count $<1000/mm^3$ [17]. In our series 20 allograft recipients had 32 granulocytopenic episodes that could be divided into severe granulocytopenia

$<1000/mm^3$ and relative granulocytopenia (1000–2000 mm^3). Using these more restrictive criteria, we found that only 8 of these 32 neutropenic episodes were temporally associated with serious infection. These observations fail to indicate a *temporal* association between severe granulocytopenia and infection alone, even though these 20 allograft recipients in the study with one or more episode of granulocytopenia did have a higher incidence of serious infection than those recipients who were never granulocytopenic in their clinical course ($p < 0.01$).

The observation that rejection predisposes to infection through alteration in humoral immunity and in some cases through rejection-mediated leukopenia or following vigorous anti-rejection therapy is frequently stated in the literature [4,18–20]. In an attempt to document this relationship in our series, the incidence of infection in 21 renal allograft recipients who had three or more rejection episodes at any time in their clinical course was compared with the incidence of infection in the 73 recipients who experienced two or fewer rejections. No statistical significance was found between these groups. However, in a prior study of this patient population, Finkelstein et al. [7] had reported that a second rejection episode within the first two months post-transplantation predisposes to increased mortality. These authors report 9 deaths or transplant nephrectomies in 12 patients with greater than two rejections while only 9 of 27 patients with no rejections died or underwent transplant nephrectomy. This data is at variance with the Belfast series, which had a lower rejection rate overall, and no deaths caused by infection within the first 60 days after transplantation. There were, however, two later deaths caused by infections which were associated with leucopenia brought about by anti-rejection therapy [13]. Nonetheless, our data appears comparable with the general experience reported in this country and Europe with approximately a 35% mortality rate associated with serious infections [4,14]. With alteration in the approach to immunosuppressive therapy there have been conflicting and changing data on the role of high dose steroids as a putative risk factor. The 39 allograft recipients we were able to evaluate represented a population too small to be evaluated statistically. However, in the present series, recipients treated with high dose steroids did have a higher mortality rate (33%) secondary to infection than the low dose group (11%).

In conclusion, analysis of our renal allograft recipient population did not establish significant temporal relationships between the potential risk factors, leucopenia, multiple rejection episodes, high dose corticosteroid therapy, and serious infections. Mortality rates associated with serious infections were definitely higher in those patients who experienced any of the assessed risk factors at some time in their course. A patient profile that includes: (1) age less than ten years or greater than 40 years; (2) a cadaveric allograft, and (3) more than two rejection episodes with inherent high dose immunosuppressive therapy, increased the risk of serious infections and mortality. No attempt was made in this study to evaluate tissue typing and antigen matches of the cadaveric recipients with the risks analyzed since this information was not standardized throughout the time period studied. This data and data on patients who receive anti-lymphocytic globulin therapy may further delineate patients at greater risk for serious infections and unsuccessful outcomes.

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