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The Practical Journal for Emergency Physicians

Emergency Medicine Reports®

Volume 25, Number 2 January 12, 2004

Human organ transplantation has made phenomenal strides since the first successful recorded transplant of a cornea in Austria in 1905.[1] Organ transplantation not only improves the quality of life in many patients but also proves to be life-saving as well. Transplant recipients have their own set of special problems that often require emergency department (ED) visits, extensive diagnostic evaluations, and frequent hospital admissions. The interplay of the patient's immunosuppressive medications, pre-existing co-morbid illnesses, potential problems with the allograft, and the occurrence of routine illness also seen in the general population make evaluation of the organ transplant recipient (OTR) a challenge even for the most skilled physicians. Typically, OTRs are followed closely by their transplant surgeons, primary care providers, and transplant coordinators, all of whom are valuable resources for the emergency physician caring for these complex patients. Emergency physicians should attempt to involve the patient's transplant team early in the decision-making process to help coordinate the timing and location of much of the diagnostic evaluation, as well as to discuss major treatment decisions.[2]

—The Editor

Evaluation and Management of Solid Organ Transplant Patients in the Emergency Department

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Organ Procurement

There are three types of donor organs based on donor source: cadaveric, living-related, and living-unrelated donors. The potential cadaveric donor pool is estimated to be about 60-80% greater than what currently is being captured. In 2001, there were 107,450 people waiting for an organ transplant; 6% of these patients died while waiting.[3-5] Several myths circulate in the general population that may dissuade many potential donors from discussing the option of organ donation with their families. (*See Table 1.*) Potential organ donors have causes of death that include intracranial bleeding, motor vehicle accidents, gunshot wounds, closed head injuries, and anoxia. Emergency physicians can play a key role in the organ donation process by identifying

potential donors. The family of any potential organ donor ideally should be approached by a trained organ procurement coordinator. (*See Table 2.*)

Problems Common to All Transplant Patients

Transplant patients are susceptible to all of the acute illnesses that affect the general population, as well as to problems related to immune suppression, such as opportunistic infections, adverse effects of the medications themselves, or increased risk of neoplasm. Various neurologic problems are seen as well. Each of the four major transplanted organs—kidney, heart, liver, and pancreas—will be discussed individually. Of note, patients with gastroenteritis require special attention, as the inability to ingest or absorb their medications may precipitate an episode of acute rejection.[6]

Emergency Medicine Reports™ (ISSN 0746-2506) is published biweekly by Thomson American Health Consultants, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Vice President/Group Publisher: Brenda Mooney
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GST Registration No.: R128870672

Periodicals postage paid at Atlanta, GA. **POSTMASTER:** Send address changes to ***Emergency Medicine Reports***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $31. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Multiple copy prices: One to nine additional copies, $359 each; 10 to 20 additional copies, $319 each.

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In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Drs. Freeman, Awad (authors), Butler, and Riviello (peer reviewers) report no relationships with companies related to the field of study covered by this CME program. Dr. Bosker (editor) is on the speaker's bureau for Pfizer, Rhone-Poulenc Rorer, and Parke-Davis. Dr. Bosker also acknowledges that he receives royalties, commissions, and other compensation relating to the sale of textbooks, reprints of articles, and other written materials to the following pharmaceutical companies: Pfizer, Genentech, Aventis, Pharmacia, and Bayer.

Infection. The majority of infections that occur in organ transplant recipients are opportunistic and are a major cause of death in the immunocompromised patient. There are three general time frames during which infection can occur in the post-transplant period: first month, second through sixth month, and after the sixth month.

Infections in the first month usually are related to surgical and technical complications and are bacterial in origin. The most common viral infection seen in the first few weeks post-transplantation is reactivation of human herpes simplex virus. After the first six months, patients usually have community-acquired infections. Patients who have chronic graft rejection and thus require higher doses of immunosuppressive medications, and patients with reactivation of chronic illnesses such as hepatitis tend to get the opportunistic infections in the late transplant period (after six months). (*See Table 3.*)

The highest incidence of fungal infections occurs during the first two months post-transplantation. Early fungal infections usually are secondary to Candida or Aspergillus species. Aspergillus infections are more aggressive and can present as pneumonia or central nervous system (CNS) infection with intracranial mass lesions. Infections can be superficial or invasive, and it's important to differentiate between them. Transplant recipients with invasive fungal infections have a very high mortality rate. Amphotericin B remains the drug of choice to treat aggressive fungal infection. Other opportunistic infections are rare during this period. Another common viral infection during the first month is reactivated varicella zoster infection.[7] Viruses (especially cytomegalovirus [CMV]) and opportunistic agents become more common in months 1-6.

Individual Organisms. *Cytomegalovirus (CMV).* CMV is the most common pathogen in transplant patients. There are three patterns of infection—primary, reactivation, and superinfection. Primary infection occurs when infected cells are transmitted from donor to recipient via transplant or transfusion. More than 50% of patients will develop disease as a result of this transmission, including pneumonia, entercolitis, or encephalitis.[8] Reactivation occurs when latently infected patients have symptomatic disease after transplant. Superinfection occurs when both the donor and recipient are infected with different strains of CMV. CMV has four major effects in transplant patients: infectious disease syndromes, leukopenia and decreased cell mediated immunity, acute and chronic rejection, and decreased long-term patient survival. CMV can affect a wide range of organ systems. The typical presentation of illness caused by CMV involves a mononucleosis-like syndrome of fever, malaise, arthralgias, myalgias, leukopenia, mild atypical lymphocytosis, and mild elevation of the transaminases. Any portion of the GI tract can be affected. Retinitis is another important manifestation of CMV infection, one that is the most difficult to treat.

The diagnosis of CMV infection most accurately is made via demonstration of viremia via polymerase chain reaction or tissue invasion via biopsy. Antibody titers typically are drawn, but these have little diagnostic value as the presence of antibodies does not necessarily indicate active disease. Treatment involves intravenous ganciclovir for 2-4 weeks.[7,8]

Table 1. Organ Donation and Transplantation Myths[9]

- If the emergency physician knows you are an organ donor, the physician will not work as hard to save you.
- Having "organ donor" noted on your driver's license or carrying a donor card is all you have to do to become a donor.
- Only hearts, livers, and kidneys can be transplanted.
- A history of medical illness means organs or tissues are unfit for donation.
- Being too old prohibits organ donation.
- If you agree to donate your organs, your family will be charged for the cost.
- Organ donation disfigures the body and changes the way it looks in a casket.
- Religion prohibits organ donation.

Table 2. Contraindications for Organ Donation[8]

- Significant disease in the organ to be transplanted
- Significant mental dysfunction in donor and/or recipient
- Significant transmissible disease (HIV, sepsis)
- ABO blood type incompatibility
- Immunologic incompatibility
- High risk of perioperative morbidity and mortality
- Malignancy other than isolated CNS
- Extreme old or young age

Epstein-Barr Virus (EBV). Epstein-Barr Virus is a herpes virus that can cause a mononucleosis syndrome, hepatitis, and post-transplant lymphoproliferative disorder. EBV causes a similar clinical syndrome to CMV. Illness from EBV usually is not seen until after six months post-transplant. Post-transplant lymphoproliferative disorder is the most severe form of EBV infection. Diagnosis of this virus may be difficult because it usually is not associated with a positive heterophile test (Monospot), splenomegaly, or pharyngitis in the transplant patient.[8]

Varicella-Zoster Virus and Herpes Simplex Virus. Primary varicella infection is a serious problem. It rapidly can disseminate and lead to pneumonia, encephalitis, pancreatitis, hepatitis, and disseminated intravascular coagulation. If an OTR who is varicella-zoster virus (VZV) seronegative is exposed to a person with chicken pox or shingles, strong consideration should be given to admission for IV varicella zoster immune globulin. Reactivation of a latent VZV infection usually only causes a cutaneous eruption, typically confined to one dermatome. Herpes simplex reactivation is common and causes oral or genital ulcers that may be treated with oral acyclovir.[6]

Immunosuppressive Drugs. There is no consensus for optimal induction immunosuppressive protocols. Several combinations of therapy are possible and vary from center to center. Most patients begin with a three-drug protocol that includes:

- A calcineurin inhibitor (cyclosporin or tacrolimus);
- A purine synthesis inhibitor (azathioprine or mycophenolate mofetil); and
- A corticosteroid (prednisone or methylprednisolone).

The risk of acute rejection and graft loss is highest in the first three months after transplantation. Therefore, the number and doses of immunosuppressive drugs should be highest at this time. The most serious side effects of immunosuppressive therapy are infection and malignancy, as well as direct organ toxicity. These side effects correlate with the total amount of immune suppression. The medications typically are tapered to maintenance levels by 6-12 months post-transplantation.

Cyclosporine. Since its introduction in the early 1980s, cyclo-sporine has been the mainstay of transplant immunosuppression. It is classified as a calcinuerin inhibitor[10] and blocks the proliferation of helper and cytotoxic T cells and inhibits lymphokine release.[11] The most significant side effect of cyclosporine is acute and chronic nephrotoxicity. Nephrotoxicity occurs in about one-third of patients. It is dose-dependent and generally is reversible after dose reduction or short-term discontinuation. Other side effects include hypertension, hirsuitism, gout, hepatotoxicity, and gingival hyperplasia. Neurotoxicity manifested by headache, hand tremors, and memory loss may be seen. The starting dose is 8-10 mg/kg/day that is tapered over six months to 3-5 mg/kg/day. Monitoring of serum levels is of limited clinical utility, but levels typically are maintained between 50 and 150 ng/mL.[8] Cyclosporine has many significant drug interactions, as noted in Table 4.

Tacrolimus (FK 506). Tacrolimus is a macrolide antibiotic derivative that also is a calcineurin inhibitor and inhibits lymphocyte activation. It initially was approved for liver transplant patients, but studies have demonstrated efficacy in renal transplant as primary or rescue therapy.[12,13] This drug has shown significant improvement in graft survival.[14] As with cyclosporine, the major adverse effect is nephrotoxicity.[12,15,16] Other adverse effects include hyperkalemia, hemolytic uremic syndrome, confusion, seizures, encephalopathy, headache, sleep disturbances, paresthesias, aphasia, and hyperglycemia. Do not give a concurrent macrolide antibiotic as this may induce acute toxicity.[17] Sirolimus is a new drug that structurally is related to tacrolimus but works at a different site of the cell signaling pathway. Unlike tacrolimus, sirolimus has no associated nephrotoxicity or hypertension. It presently is being studied for use in maintenance immunosuppression and rescue therapy for refractory acute rejection.[18] The most common side effects are thrombocytopenia and increases in serum LDH, cholesterol, and triglyceride levels.

Mycophenolate Mofetil (MMF). MMF is a newly approved synthetic derivative of a fungal antibiotic. It blocks a step in the pathway of purine synthesis. Lymphocytes are relatively dependent on the de novo pathway of purine synthesis, unlike other cells that predominately use the salvage pathway.[8] By blocking this pathway, MMF inhibits cytotoxic T cell generation. It also inhibits antibody formation. MMF has replaced azathioprine in many centers for maintenance immunosuppression, although no long-term benefit in graft survival has been shown.[19] It is effective for refractory acute rejection and may

Table 3. Infections in Transplant Patients[11]

TIME POST-TRANSPLANT	LIKELY SOURCE OF INFECTION
0-1 month	Post-surgical infection; UTIs (*Escherichia coli*), IV lines (*S. aureus*, *S. viridans*), wound infection (*S. viridans*), pneumonia (*S. pneumoniae*)
1-6 months	CMV, EBV, PCP, meningitis (Listeria), fungal sepsis
> 6 months	**Good graft function:** same as general population **Chronic infection with immune modulating viruses (i.e., hepatitis B/C):** ongoing end-organ damage **Chronic rejection:** acute and chronic opportunistic infections

Key:
UTI = urinary tract infection; CMV = cytomegalovirus; EBV = Epstein-Barr Virus; PCP = *Pneumocystis carinii* pneumonia

Table 4. Cyclosporine Drug Interactions[8]

INCREASES LEVEL	DECREASES LEVEL
Diltiazem	IV Trimethoprim sulfamethoxazole
Verapamil	Isoniazid
Nicardipine	Rifampin
Erythromycin	Phenytoin
Ticarcillin	Phenobarbital
Doxycycline	Carbamazepine
Fluconazole	Omeprazole
Ketoconazole	
Nafcillin	
Metoclopramide	
Alcohol	
FK506	

prevent chronic rejection. The dose is 2 g/day. MMF is not nephrotoxic and appears to have less bone marrow suppressive effects than azathioprine. The major side effects typically are mild and include gastritis, esophagitis, nausea, and diarrhea. Use caution when using magnesium or aluminum antacids to treat the gastrointestinal (GI) symptoms, as they interfere with the absorbtion of MMF.[6]

Corticosteroids. Corticosteroids alter T cell proliferation, inhibit cytokine production, suppress macrophage function, and induce lymphocyte apoptosis. Intravenous pulse methylprednisolone is the first-line therapy for acute uncomplicated allograft rejection. The dose is 500-1000 mg/day for 3-5 days as pulse therapy. Oral therapy then is restarted with a rapid taper back to maintenance levels, which usually are 10 mg/day. The major, long-term side effects of steroids include avascular bone necrosis, hypertension, adrenal suppression, cataracts, GI bleeding, glucose intolerance, delayed wound healing, and psychiatric disturbances.

Azathioprine. Azathioprine is a purine analog anti-metabolite derivative that is a bone marrow toxin. It blocks activation of T-lymphocytes and inhibits lymphocyte replication and function by inhibiting DNA synthesis. The typical dose is 2 mg/kg/day. The major side effects are leukopenia, thrombocytopenia, hepatotoxicity, and increased risk of neoplasm. Other adverse effects include alopecia, pancreatitis, rash, and GI upset.

Antilymphocyte Monoclonal Antibody Preparations. Antilymphocyte serum (ALS) is made from immunizing rabbits or horses with human lymphoid cells derived from the thymus or cultured B cell lines. It is used as primary treatment for and prophylaxis against acute rejection. The dose is 10-15 mg/kg/day for 7-10 days. The side effects include fever, chills, and, rarely, anaphylaxis.

OKT3 is the only mouse antibody that is licensed for antirejection therapy. It inhibits T-cell mediated immunity. It is used for primary therapy for acute rejection and as rescue therapy for resistant rejection. The typical dose is 5 mg IV per day for 10-14 days. The adverse effects include increased risk of infection, especially CMV and EBV. The first dose is associated with fever, chills, vomiting, diarrhea, hypotension, chest pain, and wheezing. Serious complications include fatal pulmonary edema, graft thrombosis, and graft loss.

Cancer. Malignancy is common in long-term OTRs. The chronic use of immunosuppressive drugs increases this risk. The types of cancers encountered in OTRs are different from those in the general population. There is a much higher incidence of squamous cell skin cancer; non-Hodgkin's lymphoma; Kaposi's sarcoma; cancer of the cervix, vulva, and perineum; hepatobiliary cancer; and various sarcomas.[20] The malignancies that are most common in the general population—lung, breast, prostate, and uterine—are not seen in increased frequency in OTRs.[21] Overall, the most common post-transplant cancers are those of the skin and lips, which are seen in one-third of patients.[20,21] Lymphoproliferative disorders, ranging in severity from lymphoid hyperplasia to non-Hodgkin's lymphoma, comprise about 20% of all post-transplant malignancies.[22]

Neurologic Complications. Neurologic complications occur in 30-60% of patients receiving solid organ transplants.[23] These include CNS infection, encephalopathy, seizure, stroke, and peripheral neuropathy.[24] CNS infection most often presents as meningitis, encephalitis, and brain abscess. The most common causative organisms are *Listeria monocytogenes*, *Aspergillus funigatus,* and *Cryptococcus neoformans*. Drugs such as tacrolimus and cyclosporine can cause encephalopathy that mimics CNS infection.[23] Immunosuppressive therapy reduces the inflammatory response to infection, thus the response to infection often is blunted in transplant patients. They typically have headache, altered mental status, or fever without focal deficits. However, focal deficits may occur in association with aspergillosis, toxoplasmosis, or fungal abscess.[23] Lumbar puncture strongly should be considered for patients with new

Table 5. Most Common Diagnoses in Patients Requiring a Renal Transplant[5]

Glomerular diseases	24%
Diabetes	20%
Hypertensive nephrosclerosis	14%
Polycystic kidney disease	9%
Tubular and interstitial diseases	5%

Table 6. Causes of Late Post-Transplant Graft Dysfunction[29]

- Obstruction
- Cyclosporine nephrotoxicity
- Other drug-related nephrotoxicity: ACE inhibitors, trimethoprim
- CMV infection
- Renal artery stenosis: uncommon, usually causes severe hypertension
- Recurrent primary disease, especially glomerulonephritis and metabolic disorders
- Hypertension
- Pyelonephritis
- Rejection

headache, fever, or altered mental status. Computed tomography (CT) of the brain is indicated before lumbar puncture in patients who are obtunded or have focal deficits. Spinal fluid should be tested for the usual studies, as well as fungal cultures, cryptococcal antigen, and polymerase chain reaction (PCR) viral assays.

Renal Transplant

Overview. Renal transplants are the most common solid organ transplants in the United States. In 2001, there were 23,848 solid organ transplants, of which 59% were kidneys.[5] However, more than 64,000 patients were on the waiting list for a kidney in 2001, and almost 5% of the patients died while awaiting a kidney. The most common diagnoses in patients who required a renal transplant are listed in Table 5. The waiting time for a cadaveric renal transplant varies from 422 days to 1453 days, depending on the recipient's blood type.[25] Graft prognosis is directly related to the source of the donor kidney. Presently, one-year cadaveric graft survival rates are greater than 90%.[25] However, recipients from living related donors have lower mortality rates than recipients from cadaveric donors. This is multifactorial, however, depending on the donor and the recipient. Patient survival after a cadaveric renal transplant is 80% at five years, but rises to 90% at five years with a living donor.[5]

Transplant Procedure. The allograft usually is placed extraperitoneally in the recipient's iliac fossa. The left iliac fossa often is avoided in recipients older than age 40 because of the prevalence of diverticulosis in this age group and problems with confusing diverticulitis with acute inflammation of the transplanted kidney.[8] The nonfunctional kidney usually is not removed.

Complications. The most common causes of death in renal transplant recipients (RTRs) are cardiovascular disease, infection, and cancer.[1] Patient death is the second most common cause of graft failure, often as a result of morbidity acquired before transplantation. The major causes of morbidity after transplantation, aside from rejection, are: hypertension (46%), cataracts (24%), avascular necrosis (18%), malignancy (14%), urinary tract infection (17%), pneumonia (9%), steroid-induced diabetes (6%), chronic hepatitis (6%), peptic ulcer disease (4%), diverticulitis (3%), myocardial infarction (4%), and stroke (2%).[26] (Patients may have more than one cause of morbidity.)

Post-Surgical Complications. *Urine.* Most surgical complications present in the early post-transplant period. A common early complication is ureteral obstruction, resulting in painless, decreased urine flow. Causes of this include blood clots, stones, ureteral necrosis, or intraoperative technical problems. The diagnosis is made via demonstrating dilatation of the urinary collecting system via ultrasound. Urine leakage usually presents in the first few post-operative weeks and is a serious complication that can lead to infection and death. It usually is due to necrosis of the distal ureter. The most common reason for this is interruption or thrombosis of the ureteral artery due to damage incurred during the donor nephrectomy. Other causes include infection or clot retention, leading to acute bladder distention. Clinically, the patient presents with symptoms that may mimic acute rejection, including allograft tenderness, fever, and abdominal swelling. Urine flow will remain unchanged initially. The diagnosis is made via ultrasound demonstrating a perinephric fluid collection. Treatment involves placement of a percutaneous nephrostomy tube followed by ureteral repair.

Bleeding and Lymphatic. Hematuria is common in the first post-operative week and usually resolves without intervention. Later on, it may be associated with rejection. Painful hematuria may be due to leakage of small vessels in the renal hilum or perinephric fat. Urgent surgical exploration is indicated in that case.

Lymphocele is a fairly common complication that occurs when lymph collects in the retroperitoneal space if the lymphatic vessels are not ligated carefully at the time of surgery. Diagnosis is made via ultrasound and often is managed by laparoscopic drainage.

Vascular. Renal artery thrombosis is reasonably uncommon but can cause decreased renal function, usually between three months and two years post-operatively. The etiology usually is technical, but it may develop as a result of immunologic complications. The diagnosis is confirmed by angiography.[27]

Rejection. Approximately 15-20% of renal transplant patients have recurrent episodes of acute rejection.[8] Rejection is divided into three categories: hyperacute, acute, and chronic, although there are overlapping features and transitions among these categories.

Hyperacute rejection occurs in the operating room within minutes of revascularization. The kidney becomes cyanotic and

Table 7. Most Common Infectious Causes of Death in Renal Transplant Recipients[8]

- Pneumonia
- Sepsis
- Peritonitis
- Meningitis

Table 8. Causes of Early (1-12 Week) Graft Dysfunction[8]

- Acute rejection
- Cyclosporine nephrotoxicity
- Urinary tract obstruction
- Recurrence of primary renal disease
- Infection

aggressive graft destruction ensues. This form of rejection consists of an immunologic cascade that involves platelet aggregation, degranulation, and microvascular obstruction.[8,28] This form of rejection usually is correlated with the presence of preformed circulating antibodies against donor antigens. Hyperacute rejection is rare today, as the antibodies readily can be identified in a pretransplant crossmatch.

Most patients have at least one episode of acute rejection in the days and weeks post-transplantation.[8] The classic presentation of acute rejection includes fever, malaise, oliguria, hypertension, and tenderness over the allograft. Laboratory abnormalities include proteinuria, hematuria, red blood cell casts, leukocytosis, and increased creatinine.[28] However, many of these symptoms rarely are seen in patients on the newer immunosuppressive agents. Impaired renal function often is the only finding. The pathophysiology is cellular infiltration with lymphocytes and macrophages followed by vascular involvement. The usual method of evaluating a patient with possible acute rejection is radioisotope perfusion scan to exclude other conditions. A biopsy may be needed for definitive diagnosis. When acute rejection is diagnosed, anti-rejection therapy, including steroids, ALS, and OKT3, is initiated.

Chronic rejection, also known as chronic allograft nephropathy (CAN), is defined as a progressive decline of graft function that is not caused by the interruption of immunosuppressive mediations, recurrence of renal disease, or surgical complications.[30] CAN is the most frequent cause of graft failure today. Chronic rejection typically presents as hypertension, a progressive increase in creatinine, and proteinuria. Many factors play a role in CAN, including under-immunosuppression, poor compliance, drug toxicity, ischemia-reperfusion injury, and HLA incompatibility.[30] Table 6 contains common causes of late post-transplant graft dysfunction.

Cardiovascular Disease. Cardiovascular disease accounts for 36% of total mortality in renal transplant recipients.[31] Cardiovascular disease develops about 20 years earlier in transplant recipients than in the general population.[32] Hypertension is extremely common in renal patients, with a 60-100% prevalence.[33] Pre-transplant hypertension is a strong predictor of post-transplant hypertension. The most common cause of post-transplant hypertension is impaired renal function associated with chronic allograft dysfunction.[34] Post-transplant hypertension can be treated with calcium channel blockers, beta-blockers, diuretics (except potassium-sparing), or angiotensin-converting enzyme inhibitors. Hyperlipidemia is a well-known feature of renal transplant recipients and contributes to the development of cardiovascular disease. Renal disease is associated with significant abnormalities in lipid metabolism. Factors that influence post-transplant hyperlipidemia include age, body weight, pre-transplant lipid levels, proteinuria, and allograft dysfunction.[35]

Infection. The most important risk factor for post-transplant infections is the intensity of immunosuppression. Infection accounts for the most common causes of death in renal transplant patients, as noted in Table 7. Age, malnourishment, long duration of dialysis, presence of infectious foci, and hepatitis B virus or hepatitis C virus positivity are predisposing factors for post-transplant infection.[36] Factors that influence risk of infection include exposures and state of immunosuppression, as well as indwelling catheters, malnutrition, uremia, hyperglycemia, and infection with immunomodulating viruses such as EBV, herpes simplex virus (HSV), hepatitis C virus, or human immunodeficiency virus (HIV).[37]

Bacterial Infections. Urinary tract infections (UTIs) are common post-transplant, especially in the first year. UTIs presenting in the first three months post-transplant frequently are associated with overt pyelonephritis and bacteremia. There is a lower rate of pyelonephritis later in the transplant course unless anatomic or functional abnormalities of the urinary tract are present. Patients presenting with urosepsis in the late post-transplant period have a high likelihood of stone disease.[7] The pathogens are similar to what is seen in the general population, including *Escherichia coli*, enterococci, and *Pseudomonas aeruginosa*. Transplant recipients are susceptible to developing pyelonephritis and/or sepsis. Patients usually are on trimethoprim-sulfamethoxazole for the first year. Infections can be treated with quinolones, and admission strongly should be considered. Many patients are maintained on antibiotic prophylaxis, so many of the infecting organisms have multiple drug resistances, and urine cultures are indicated prior to treatment. Salmonella commonly is seen in RTRs. The annual incidence of nonthyphoid salmonella in RTRs is 20 times that in the general adult population. The most common presentation is febrile illness with bacteremia.[7,38] It also may cause a variety of localized infections, such as UTIs, gastroenteritis, soft-tissue abscesses, and pneumonia.[7]

Emergency Department Evaluation. In addition to the history taken for all OTRs, the patient should be questioned about baseline body weight, creatinine and cyclosporine level, as well as urine output. Physical exam should focus on volume status and overall patient stability. The allograft should be palpated for swelling, and tenderness. The abdomen and incision should be examined for erythema and drainage.

Table 9. Ultrasound Findings in Acute Rejection[8,47]

- Increase in volume of the graft outside the normal range
- Enlarged and abnormally echo-poor pyramids that result in a more distinct cortico-medullary boundary
- Alternating echo-poor and echo-bright regions within the cortex due to hemorrhage or infarction
- Perirenal fluid collections

Table 10. Etiology of Heart Failure in Transplant Patients[11]

Coronary artery disease	45%
Dilated cardiomyopathy	46%
Valvular	3.5%
Retransplantation	2%
Congenital	2%
Miscellaneous	2%

Causes of early graft dysfunction are difficult to differentiate clinically, but there are some common treatable causes of early graft dysfunction, as noted in Table 8.

In addition to routine laboratory testing, the most useful specialized diagnostic study that readily can be obtained from the ED is a renal ultrasound. Ultrasound is a useful modality, however, because of its availability and lack of nonionizing radiation or contrast injection. Duplex doppler ultrasound, although non-invasive, is neither sufficiently sensitive nor specific to make the definitive diagnosis of acute rejection.[39] Ultrasonographic findings of acute rejection are debated, but the ones that generally are accepted are noted in Table 9.

Perirenal fluid collections may consist of urine, lymph, blood, or pus. They may be associated with rejection, post-surgical complications, or a UTI. Physical exam in a patient with a perirenal fluid collection may reveal suprapubic swelling, drainage from the wound, edema over the graft, and ipsilateral leg edema.

Treatment. The most life-threatening complications that an RTR may present with in the ED are overwhelming infection and acute graft failure. Serious infection may lead to acute decompensation in a seemingly stable patient. Broad-spectrum antibiotic coverage should be initiated (after appropriate cultures are taken) whenever a significant infection is suspected. Acute graft failure may lead to life-threatening hyperkalemia or volume overload with resultant pulmonary edema and respiratory decompensation. Both of these conditions may require emergent dialysis.

Heart Transplant

Overview. The first human heart transplant was performed by Christian Barnard in Capetown, South Africa, in 1967.[40] There are approximately 2000 heart transplants performed each year. One-year survival is 85%, up from 15% when the procedure first was developed. Five-year survival is 70%.[5,40] There were 7318 patients waiting for heart transplants in 2001; 8.5% of these patients died while waiting.[5] The most frequent indications for cardiac transplant are ischemic coronary artery disease and cardiomyopathy.[41] (*See Tables 10 and 11.*)

Transplant Procedure. The current technique for orthotopic heart transplantation involves a median sternotomy incision, and the patient is placed on cardiopulmonary bypass. A large portion of the posterior wall of the right and left atrium is left in the recipient, and the donor heart is implanted via the atria and end-to-end anastomosis of the aorta and pulmonary artery. There often is venous anastomsis at the level of the superior and inferior vena cavae and pulmonary veins. The procedure typically takes 45-80 minutes. Temporary pacer wires and chest tubes usually are placed.[42]

Physiology. The transplanted heart typically is completely denervated, but it is thought that partial renervation occurs by one year.[42] The heart has a baseline rate of 100-110 bpm, without vagal parasympathetic tone. The heart rate increases in response to exercise or stress, but this is due to circulating catecholamines. Acceleration and deceleration of the heart rate occurs more slowly than in the native heart. Respiratory arrhythmia and sinus-mediated reflex bradycardia do not occur. Unless rejection is present, arrhythmias are uncommon.

Complications. Infection and rejection are common causes of mortality in the first year. The most common ED complaints of heart transplant recipients (HTR) are fever (37%), shortness of breath (13%), GI (i.e., nausea, vomiting, and diarrhea) (10%), and chest pain (19%). The most common ED diagnoses to rule out are sepsis (18%), rejection (11%), and pneumonia (8%).[43]

Infection. In most centers, infectious complications are the most common cause of death after transplantation.[41] Infections in the first month commonly are bacterial and usually pulmonary. Nosocomial organisms such as Legionella, Pseudomonas, and Proteus often are culprits. Other typical causes of post-operative infection, such as UTIs and bacteremias, are seen as well. Late post-transplant infections often are due to opportunists such as CMV, herpes, *Pneumocystis carinii,* and fungi.

Rejection. Almost every patient experiences some acute rejection episode during the first transplant year. The signs and symptoms may be subtle and easily overlooked. Generalized fatigue and arrhythmias may be the only findings. Sinus tachycardia may reflect hypovolemia, hypoglycemia, rejection, silent myocardial infarction (MI), pulmonary adrenal insufficiency, cardiac tamponade, or an abdominal process that is being masked by corticosteroids.[41] Atrial arrhythmias, especially atrial flutter, may signal rejection. Ventricular arrhythmias may be seen in severe rejection or ischemic disease. Most episodes of rejection are not clinically detectable, so surveillance endomyocardial biopsies routinely are done.

Coronary Artery Disease. The major long-term problem after transplantation is the development of coronary artery disease in the transplanted heart. Chest pain in HTRs rarely is related to cardiac ischemia because the denervated heart is incapable of producing angina.[6,44] Ischemia often presents as congestive heart failure, ventricular arrhythmias, hypotension, syncope, or sudden death.[45,46] The cause of graft coronary artery disease

Table 11. Contraindications to Heart Transplant[41]

- Advanced age (> 70 yr)
- Irreversible hepatic, renal, or pulmonary dysfunction
- Severe peripheral vascular disease or cerebrovascular disease
- Insulin-requiring diabetes mellitus with end-organ damage
- Active infection
- Recent cancer with uncertain status
- Psychiatric illness with poor medical compliance
- Systemic disease that significantly would limit survival or rehabilitation
- Pulmonary hypertension with increased pulmonary vascular resistance

(CAD) is controversial and is probably multifactorial, with immunologic factors being important. Development of CAD may reflect chronic rejection.[41]

Emergency Department Evaluation. *Cardiac Evaluation.* The ausculatory exam of an HTR often is unrevealing. An S3 or S4 may reflect cardiac failure. Irregular rhythms will present with arrhythmias. There may be crackles or rales present in congestive failure with varying degrees of respiratory distress. Peripheral edema may be present as well. The electrocardiogram (ECG) should demonstrate sinus rhythm. The ECG will reflect electrical activity from the recipient as well as from the donor's heart. Both sinus nodes will produce distinct P waves. Sinus dysfunction may appear in the early post-operative period and usually is self-limited. Some patients, however, may require treatment with theophylline or a permanent pacer. Chest radiographs should be normal. Apparent cardiomegaly may be due to transplantation of a donor heart that was larger than the recipient's heart. Cardiac enzymes may be elevated during rejection or ischemia.[6,11]

Treatment. The main cause of death after the first transplant year is chronic rejection from accelerated allograft arteriosclerosis.[48] Due to lack of native innervation, transplanted hearts will not respond to atropine or carotid sinus massage or other vagal maneuvers. Atrial dysrhythmias can be treated with digoxin or calcium channel blockers. Ventricular rhythms may be refractory, but lidocaine or similar agents may be tried. If the rhythm is unstable, cardioversion should be considered as well as 1 g of methylprednisolone IV for adrenal insufficiency.

A high level of suspicion for infectious complications should be maintained. The first three months post-transplant is the most vulnerable period for serious infections. Life-threatening infection is rare after one year due to the typically lower level of immune suppression used. All patients with fever should have an aggressive evaluation, including complete blood count, electrolytes, chest radiograph, urinalysis, blood and urine cultures, and CT of the brain, and lumbar puncture in selected patients. Broad-spectrum antibiotics should be given after cultures are drawn. Endocarditis prophylaxis is indicated before procedures such as abscess drainage or urethral catheterization. (*See Table 12.*)

Table 12. Indications for Admission of a Heart Transplant Patient[5,6,41]

- Congestive heart failure
- Fever
- Shortness of breath
- Hypoxia
- Poorly controlled hypertension
- New arrhythmia

Liver Transplant

Overview. Orthotopic liver transplantation has been established as effective therapy for both acute and end stage liver disease. In 2001, there were 18 transplants per million population,[49] making it the second most common solid organ transplant procedure. The five-year survival for recipients from cadaveric donors is 72%, while it is 86% for recipients from living donors. The median time to transplant was 770 days, and 7% of patients died while waiting for a liver.[5] (*See Tables 13 and 14.*)

Transplant Procedure. The harvested liver functions best if ischemia is limited to 8 hours, but it can tolerate up to 24 hours cold ischemia. A cholecystectomy is performed on the donor liver prior to transplantation. The recipient's diseased liver is removed. The donor liver is anastomosed to the suprahepatic inferior vena cava, the infrahepatic vena cava, hepatic artery, and portal vein to secure it an orthotopic position. After reperfusion of the liver, the final anastamosis is performed, which is the bile duct. Biliary reconstruction is done via choledochocholedochostomy with T tube placement. The T tube typically is left in place for three months. Alternatively, a Roux-en-Y loop with a choledochochojejunostomy may be performed, especially if the patient has intrinsic biliary disease. Early bile production is most indicative of graft function.[2]

The first successful living-donor liver transplant was performed in 1989 using the left hepatic lobe. Since 1994, right hepatic lobe transplantation has become more prevalent because it is smaller. Advantages of a living donor transplant include performing the transplant before the clinical condition deteriorates and markedly decreased cold ischemia time. The main disadvantage is the risk to the donor.[50] One-year patient survival rates are close to 90%.

Infectious Complications. Mortality related to infections in liver transplant patients decreased from more than 50% in the 1980s to less than 10% in the 1990s.[51] Most infections occur during times of peak immunosuppression, and the majority are seen during the first two months post-transplant.[52] The most common infections after orthotopic liver transplant are bacterial infections of the liver, biliary tract, peritoneal cavity, blood, and laparotomy wound.[53]

The risk of infection is highest soon after surgery. Early post-operative infections usually are related to surgical complications, initial graft dysfunction, or preexisting morbid conditions.

Biliary tract infections include cholangitis, abscesses, peritonitis, or wound infections.

Table 13. Most Common Diagnoses in Patients Requiring Liver Transplant[28]

- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Fulminant and subfulminant hepatitis
- Cirrhosis due to hepatitis B or C virus (most common)
- Alcoholic liver disease
- Biliary atresia and metabolic diseases
- Hepatocellular carcinoma

Table 14. Contraindications for Liver Transplantation[28]

- Extrahepatic malignancy
- Liver metastases
- Extrahepatic organ failure
- Noncompliance
- Active substance abuse
- AIDS
- Uncontrolled systemic infection

Patients are the most immunosuppressed at the first month post-transplant. Infection is primarily bacterial, specifically gram-negative enteric organisms, but infections often are polymicrobial. In the first month, patients also may present with nosocomial pneumonia or with urinary tract infections secondary to intubation or indwelling bladder catheterization. Meningitis due to organisms including *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Listeria monocytogenes*, and gram-negative rods also is seen. Fungal infections occur most often in the early post-operative period and may present as disseminated multi-organ infection, peritonitis or asymptomatic colonization, or fungemia.[2] *Candida albicans* is the most common fungal pathogen seen.[54]

Active CMV infection is seen in 35% of liver transplant recipients (LTRs), usually in the first 1-2 months post-transplant. Infection of the blood or graft is the most common presentation.[2] Recurrence of hepatitis B or C is common. Eighty-six percent of allografts are reinfected with HBV, and half of those patients lose their graft as result.[49]

Postoperative Complications. In addition to problems due to systemic infection, rejection, and immunosuppressive drug effect, postoperative complications that could be seen in the ED are most commonly a result of bleeding, biliary, vascular, and wound complications.

Bleeding. Intra-abdominal hemorrhage occurs postoperatively in 7-15% of patients and requires exploration in approximately 50% of cases.[55] Post-operative bleeding usually is the result of failure of a vascular anastomosis. These patients usually present while still in the hospital. Emergency physicians are most likely to encounter patients with GI bleeding, most commonly three months post-transplant, and caused by ulcers, viral enteritis, portal hypertensive lesions, or Roux-en-Y bleeds.[56] Endoscopy remains the best diagnostic tool for establishing the source of upper GI bleeding and management is in the standard fashion.[2] GI bleeding also may signal graft dysfunction, and the patient may have profound hypoglycemia and progressive coagulopathy.[2,11] Lower GI bleeding after transplantation often is secondary to colitis. CMV, *Clostridium difficile*, and fungi usually are responsible for the colitis.

Vascular Complications. In the immediate postoperative period, thrombosis of the hepatic artery or the portal vein is of concern. It occurs in 2-12% of liver transplants.[57] Hepatic artery thrombosis (HAT) can occur, leading to biliary obstruction, liver infarction, or both. Patients may present asymptomatically because of collateral vessels or with biliary tract complications, recurrent bacteremias, abscess, or fulminant hepatic necrosis.[57] Doppler ultrasound is the initial investigation of choice, although spiral CT may be used as well. Angiography is the gold standard in diagnosis. Urgent exploration with thrombectomy and revision of the anastomosis are indicated if HAT is detected. Retransplantation usually is required if HAT occurs early postoperatively because it usually results in necrosis of the liver and/or biliary tree.

Portal vein thrombosis is far less frequent than HAT. Portal vein thrombosis may present as liver dysfunction, tense ascites, and variceal bleeding. Doppler ultrasound of the portal vein should be helpful in establishing the diagnosis.

Biliary Complications. Biliary complications occur in 8-15% of liver transplant patients with mortality rate of 10%.[58,59] Patients with biliary complications such as leaks, strictures, and obstruction may have elevated bilirubin, gammaglutamyltransferase (GGT), and alkaline phosphatase levels. These laboratory findings also may be found in sepsis, graft injury secondary to ischemia, and rejection. Patients with leaks may present with peritonitis, fever, abdominal pain, constipation, jaundice, and abdominal distention. Elevations of the transaminases and bilirubin are expected. After the first month, leaks occur with either elective or inadvertent removal of an indwelling biliary catheter.[4,11] During the first month, leaks are more severe and are more difficult to treat. If there is an associated abscess, that must be drained and the patient should be started on IV antibiotics that cover the usual biliary organisms. Ultrasound is helpful in detecting biliary dilatation, fluid collections, and thrombosis of the hepatic artery or portal vein. Cholangiography is used to evaluate for leaks or strictures. Cholescintigraphy using 99mTc-labeled hepatoiminodiacetic acid is used to look for bile leaks from the cut surfaces of the liver or from the anastomosis.[61] Obstruction to the flow of bile may occur secondary to stent obstruction, sludging, or stone formation or strictures (late). Spiral CT is useful in the evaluation of a patient with suspected biliary obstruction, but the diagnosis is made definitively with an invasive tool, such as endoscopic retrograde cholangiopancreatography (ERCP) or surgical exploration.[2]

Rejection. The liver is relatively resistant to the hyperacute rejection that sometimes destroys kidney and heart transplants.[61] Acute allograft rejection occurs 7-14 days post-transplant. The incidence of acute rejection currently is about 20-30%. Usually patients with acute rejection have no symptoms and present with only elevated transaminases and bilirubin.

Table 15. Indications for Admission in Liver Transplant Patients

- New onset graft failure
- Fever without obvious source less than one year post-transplant
- Fever in chronic rejection patient
- Persistent hypoglycemia

Symptomatic patients may experience malaise, weakness, fever, right upper quadrant pain, or change in bile color. Rejection is definitively diagnosed by percutaneous liver biopsy. Acute rejection is treated with high dose corticosteroids and sometimes antilymphocyte therapy.

Chronic rejection usually presents six months after transplantation. The incidence of chronic rejection is 5-9%,[62,63] and it is a significant cause of graft failure. Patients with chronic rejection have elevated alkaline phosphatase levels and cholestasis and may present with pruritis. Patients with chronic rejection often require retransplantation.

Emergency Department Evaluation. The emergency physician typically does not see the immediate postoperative complications since patients typically remain hospitalized for two weeks. Attention should be paid to airway, breathing, and circulation (ABCs), as patients may present in shock with sequelae of sepsis and coagulopathy or altered mental status due to hepatic encephalopathy or hypoglycemia. Skin should be examined for turgor, reflecting hydration status, jaundice, and ecchymoses. Sources of infection should be sought, even in afebrile patients. An elevated temperature may be due to rejection or drug reaction as well. The wound should be inspected for drainage, swelling, or erythema. LTRs who present to the ED with any suspected complications of the transplant should receive complete blood count, electrolytes, blood urea nitrogen (BUN), creatinine, liver function tests, amylase, lipase, blood and urine cultures, cultures of ascites if present, chest x-ray, and abdominal ultrasound with Doppler flow studies. Cultures of indwelling lines and biliary fluid (if a T tube still is present) also should be taken.

Abdominal CT to look for fluid collections should be considered. Broad-spectrum antibiotics should be started after cultures have been taken if a patient has a persistent high fever or appears toxic. (*See Table 15.*)

Pancreas Transplant

Epidemiology. In 1966, the first human pancreas transplant was performed, and the first simultaneous kidney/pancreas transplant was performed in 1967. As of October 2000, more than 16,000 pancreas transplants have been reported to the International Pancreas Transplant Registry. Of these, 11,000 were performed in the United States. Pancreas transplants can be subdivided into simultaneous pancreas and kidney (SPK), pancreas after kidney (PAK), and pancreas transplant alone (PTA). In the United States, the majority of pancreas transplant cases were SPK. PAK transplant comprises about 10% of pancreas cases, and PTA comprises about 5% of all pancreas transplant cases.

Table 16. Contraindications to Pancreas Transplant

- Uncorrectable cardiovascular disease
- Active infection
- AIDS
- Malignancy within the past 3 years
- Active substance abuse
- Recent history of noncompliance
- Psychiatric illness
- Active untreated peptic ulcer disease
- Hepatitis B surface antigen positive
- Irreversible hepatic or pulmonary dysfunction

The median waiting time for a pancreas is one year. Five-year patient survival is 78% post-transplant.[5] The most common reason for pancreas transplantation is diabetes mellitus type I. (*See Table 16.*)

Transplant Procedure. The pancreas can be preserved safely for about 12-15 hours. The recipient's failed pancreas is not removed. If a combined pancreas-kidney transplant is to be done, the pancreas usually is placed on the right side and the kidney on the left. The pancreas usually is implanted first and then the kidney. The pancreatic exocrine secretions are drained into either the small intestine or the bladder.

Clinical Islet Transplantation. Surgeons can restore the function of the pancreas with a far less invasive procedure than a pancreas transplant. This procedure involves transplantation of the islets of Langerhans that contain insulin-producing beta cells. It requires only a local anesthetic and takes about one hour. The islets are injected into the liver where they secrete insulin directly into the circulatory system to control blood sugars. A single islet transplant can achieve insulin independence.[64]

Complications. *Rejection.* Acute rejection usually occurs from approximately one week to three months post-transplantation and can be treated but eventually will lead to graft loss if left untreated. Chronic rejection occurs after three months post-transplantation and leads to progressive loss of graft function. The early diagnosis of pancreatic allograft rejection is important. Hyperglycemia, which is indicative of islet damage, is a late indicator of rejection. There are some nonspecific indicators for early rejection and these include increases in serum amylase, lipase, and anodal trypsinogen. Patients who receive a concomitant kidney transplant need to have close monitoring of kidney function because increased serum creatinine usually occurs before pancreatic damage. Patients with pancreas-alone transplants can have decreases in urinary amylase in rejection in the case of bladder-drained allografts. In patients with enteric drainage and without concomitant kidney transplant, the diagnosis of rejection must rely on serum amylase, biopsy, and hyperglycemia. Early rejection episodes usually can be reversed, but if extensive islet damage has occurred there is significantly less chance of saving the transplant. Pancreas biopsy is the most sensitive and specific method for diagnosing acute rejection of the pancreas allograft.[65] High

Table 17. Targeted Physical Exam of the Organ Transplant Recipient[11]

General: Vital signs (include orthostatic), volume status
Face: Periorbital edema (glomerulonephritis), sinus tenderness (sinusitis)
Ears: Otitis media or externa
Mouth: Thrush
Neck: Nuchal rigidity (meningitis, retropharyngeal abscess)
Lymphadenopathy: CMV, EBV, hepatitis
Skin: Rash (viral syndrome), jaundice, cellulitis
Lung: Pneumonia, pulmonary edema
Heart: Pericardial friction rub—virus, uremia
Abdomen: Peritonitis (often nonspecific), wound infection, localized tenderness
Rectal: Perirectal abscess
Extremities: Hemodialysis sites, central lines (bacteremia, cellulitis); peripheral edema (volume overload, venous thrombosis secondary to renal vein thrombosis)
Neurologic: Mental status, focal deficits

dose steroids and anti-T-cell antibodies are used in the treatment of rejection. However, steroids, cyclosporine, tacrolimus, and OKT3 all can damage islet cells.[28]

Vascular Thrombosis. Vascular thrombosis, which appears to be secondary to sluggish blood flow, is the most common nonimmunologic cause of pancreas allograft failure.[66] This usually occurs within the first seven days and almost always results in loss of the graft. Thrombosis occurs in 10-20% of pancreas transplant recipients. Risk of thrombosis is highest in pancreas after kidney transplants. Graft thrombosis can be venous or arterial. Venous thrombosis presents with significant swelling of the graft, acute onset of pain, sharp rise in serum glucose, and increased serum amylase level. It rarely is reversible.[67] Arterial thrombosis may involve the splenic artery, superior mesenteric artery, or both. The serum glucose acutely rises and serum amylase level decreases. The patient with superior mesenteric artery thrombosis presents with gray urine and develops a urine leak from the duodenal segment. There is no abdominal pain or discomfort.

Metabolic Acidosis. In the immediate postoperative period, metabolic acidosis occurs as a result of release of vasoactive pancreatic peptides secondary to cold ischemia in the graft and dehydration. This usually resolves within days with IV bicarbonate administration except for patients with bladder-drained pancreas graft. In those patients, metabolic acidosis persists because of large amounts of bicarbonate loss through the urine. Blood glucose levels approach normal values within 12-24 hours and normalize within several days after transplantation.

Pancreatitis. In the early post-transplant period, allograft pancreatitis occurs in about 10-20% of patients.[28] There are many predisposing factors and these include donor abnormalities such as hemodynamic instability and vasopressor administration, procurement injury, perfusion injury, ischemic damage, and reperfusion injury. When pancreatitis occurs several weeks postoperatively, it most likely is due to reflux of urine into the pancreatic duct of a bladder-drained pancreas. Typically patients present with tenderness over the graft site, low grade fever, and increased amylase level. Serum amylase and lipase levels may not accurately reflect the degree of pancreatitis. Pancreatitis also may result from constipation, abdominal distention, and ileus called reflux pancreatitis. Reflux pancreatitis is treated with continuous bladder drainage, intravenous fluid (IVF), antibiotics, and decreased oral intake.

Allograft pancreatitis can be difficult to differentiate from other complications, such as extravasation of pancreatic juice, extravasation of urine or enteric contents, or even rejection.

Fistula and Abscess. Patients who are bladder-drained and develop leaks may have abdominal pain and tenderness along with ileus, leukocytosis, elevated amylase and lipase, and abnormalities on CT scan. In patients who have leaks, Foley-catheter decompression can be used. Patients may require enteric conversion, however, if the leaks are large or persistent.

A small bowel leak is much worse than leakage of urine because of microbial contamination and activation of pancreatic proenzymes. Small bowel leaks may occur early or late after surgery. Early leaks usually occur from technical problems or ischemia, while late leaks usually are secondary to rejection or infection. Late leaks sometimes may develop from ischemia at the duodenal staple line.[68]

Anastomotic leaks can lead to formation of an external pancreatic fistula with discharge of clear fluid and peripancreatic abscess. Patients may present with fever, tenderness of graft, and leukocytosis. If an exterior fistula develops, a high amylase content in the drainage and erythema of the skin due to contact with digestive enzymes usually is present. An ultrasound or CT scan may be used to confirm the diagnosis. Intrapancreatic abscess can develop several weeks post transplantation and may be due to chronic rejection or viral infection. Patients may present with persistent fever, pain over the graft site, and the gradual development of hyperglycemia. Serum amylase levels should not rise. Pancreatectomy is necessary for intrapancreatic abscess.

Urologic Complications. Urethritis, urethral disruption, hematuria, and recurrent urinary tract infections are very common in bladder-drained recipients. Pancreatic exocrine secretions irritate and inflame the bladder mucosa, resulting in hematuria and discomfort that may become chronic. Chronic acidosis from bicarbonate losses also is a major disadvantage of bladder-drained recipients. Urethritis usually resolves with Foley catheter drainage. Some patients eventually may need to be converted to enteric drainage to avoid scarring or disruption of the urethra. Hematuria sometimes may respond to bladder irrigation.

Emergency Department Evaluation. Pancreas transplant patients who present with a suspected complication of the transplant should have a complete blood count, electrolytes, BUN, creatinine, amylase, lipase, blood and urine cultures, chest radiograph, and urinalysis. A urinary amylase level also should be obtained in patients with a bladder-drained allograft. Abdominal ultrasound or CT should be obtained if intrapancre-

atic abscess is suspected. An arterial blood gas is indicated if acidosis secondary to bicarbonate losses is suspected in bladder-drained patients.

General Evaluation of the Transplant Patient

History. The presence of a recent fever is one of the most important portions of the history that should be obtained. Fever is the most common reason for an OTR to present to the ED.[69] However, fever can be masked by steroids, hyperglycemia, or uremia, so the absence of fever does not equal the absence of infection in these patients.[11] The date of the transplant surgery should be noted, as this helps create a time frame to determine the most likely sources of infection. Graft source is important as well, since cadaveric donor recipients have more complications than do living-related recipients. History of previous episodes of rejection should be noted, as this gives an indication as to the overall health of the graft, and the patient may say that the present symptoms are "just like my last episode of rejection." Obtain the patient's list of medications and note any changes in drugs or doses. Determine if the patient has taken his medications for that day. Note any new medications, either prescription or over-the-counter. The presence of chronic infections, especially CMV or hepatitis B/C, should be noted as well as any recent exposures to sick contacts. Lastly, attempt to determine the patient's baseline blood pressure and determinants of organ function, such as creatinine, bilirubin, or ejection fraction.

Physical Examination. If infection is suspected, the patient should be examined from head to toe, with a focus on identifying not only routine sources of infection, but uncommon sources, such as the head, neck, perineum, and rectum. Evidence of allograft failure should be sought as well as possible drug adverse effects or malignancy. See Table 17 for examination.

Diagnostic Evaluation. Any OTR with fever should receive a complete blood count, electrolytes, glucose, BUN, and creatinine, urinalysis, chest radiograph, and cultures of the blood and urine. A low index of suspicion should be maintained for meningitis; lumbar puncture with spinal fluid analysis and cultures should be obtained in high-risk patients. Organ-specific testing is indicated for suspicion of an allograft-related complication.

Disposition. Organ transplant recipients are complex patients in whom seemingly simple problems may pose serious risk to survival of the allograft or even the patient. Consultation with the patient's transplant physician and transplant coordinator or local transplant specialist strongly is recommended before any disposition decisions are made. OTRs have a much higher rate of hospitalization than the average ED patient[2] and consideration should be given to transfer the patient to a transplant center if inpatient care is necessary.

Accessing the severity and possible causes of an acute illness in an OTR as well as stabilizing the patient's condition and transferring the care of these patients to their primary transplant team should be the goal of ED management.[2]

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Emergency Medicine Reports
CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- apply state-of-the-art diagnostic and therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur.

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Physician CME Questions

11. Which of the following statements about hepatic artery thrombosis is *not* true?
    A. It can lead to biliary obstruction and/or liver infarction.
    B. Patients may present asymptomatically because of collateral vessels.
    C. Angiography is the initial investigation of choice.
    D. Urgent exploration with thrombectomy and revision of the anastomosis are indicated if HAT is detected.
    E. Retransplantation usually is required if hepatic artery thrombosis occurs early postoperatively.

12. Which of the following statements is true regarding pancreas transplants?
    A. Hyperglycemia, which is indicative of islet damage, is an early indicator of rejection.
    B. Patients who receive a concomitant kidney transplant need to have close monitoring of kidney function because increased serum creatinine usually occurs before pancreatic damage.
    C. Ultrasound is the most sensitive and specific method for diagnosing acute rejection of the pancreas allograft.
    D. Steroids, cyclosporine, tacrolimus, and OKT3 have not been shown to damage islet cells.
    E. Patients with pancreas-alone transplants can have increases in urinary amylase in rejection in the case of bladder-drained allografts.

13. Metabolic acidosis may persist in patients with pancreas transplant because of large amounts of bicarbonate loss through the urine.
    A. True
    B. False

14. Post-transplant pancreatitis may result from:
    A. constipation.
    B. abdominal distention.
    C. ileus.
    D. all of the above.

15. Which of the following regarding pancreas transplant is *not* true?
    A. Bladder-drained recipients may require enteric conversion if the leaks are large or persistent.
    B. Urethritis, urethral disruption, hematuria, and recurrent urinary tract infections are very common in bladder-drained recipients.
    C. Urethritis usually resolves with Foley catheter drainage.
    D. Intrapancreatic abscess can develop several weeks post-transplantation and may be due to chronic rejection or viral infection.
    E. Pancreatectomy rarely is indicated for intrapancreatic abscess.

16. Which of the following is the most common solid organ transplanted in the United States?
    A. Kidney
    B. Liver
    C. Heart
    D. Intestine

17. Regarding infection in organ transplant recipients, which of the following statements is true?
    A. Infections during the first month post-transplant usually are due to opportunistic organisms.
    B. The most common viral agent affecting OTRs is CMV.
    C. Salmonella is an uncommon infection in renal transplant recipients.
    D. Broad spectrum antibiotics should be withheld in the febrile transplant patient until a source of infection is identified.

18. Of the following immunosuppressive medications, which usually has mild side effects?
    A. Cyclosporine
    B. Steroids
    C. Tacrolimus
    D. Azathioprine
    E. MMF

19. Which of the following malignancies is more common in organ transplant recipients than in the general population?
    A. Uterine
    B. Colon
    C. Non-Hodgkin's lymphoma
    D. Lung
    E. Breast

20. Which statement about cardiac transplant recipients is true?
    A. The most common reason for needing a heart transplant is valvular disease.
    B. The transplanted heart will respond to atropine.
    C. Coronary artery disease manifests as anginal chest pain.
    D. The main cause of death after the first post-transplant year is chronic rejection from accelerated allograft arteriosclerosis.
    E. The electrocardiogram will not demonstrate a sinus rhythm.

In Future Issues:

Management of Esophageal Foreign Bodies in the Pediatric Population

CME Answer Key

11. C	16. A
12. B	17. B
13. A	18. E
14. D	19. C
15. E	20. D

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion.* When your evaluation is received, a certificate will be mailed to you.

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You and your facility waited more than a year for the final revisions to the Emergency Medical Treatment and Labor Act (EMTALA), but are they really good news?

EMTALA: The Essential Guide to Compliance from Thomson American Health Consultants, publisher of *Emergency Medicine Reports*, *ED Management*, *ED Legal Letter*, and *Hospital Risk Management*, explains how the changes to EMTALA will affect emergency departments and off-campus clinics. In-depth articles, at-a-glance tables, and Q-and-As on real-life situations are presented, and key differences between the "old" EMTALA and the new changes are succinctly explained.

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- How does EMTALA apply to inpatients admitted through the ED?
- What are the rules concerning off-campus clinics?

Edited by **James R. Hubler, MD, JD, FACEP, FAAEM, FCLM**, attending physician and clinical assistant professor of surgery, Department of Emergency Medicine, OSF Saint Francis Hospital and University of Illinois College of Medicine, Peoria, and reviewed by **Kay Ball, RN, MSA, CNOR, FAAN**, Perioperative Consultant/Educator, K&D Medical, Lewis Center, OH, *EMTALA: The Essential Guide to Compliance* draws on the knowledge and experience of physicians, nurses, ED managers, medicolegal experts, and risk managers to cover the EMTALA topics and questions that are most important to you, your staff, and your facility.

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Emergency Medicine Reports
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Management of Transplant Patients

Organ Donation and Transplantation Myths

- If the emergency physician knows you are an organ donor, the physician will not work as hard to save you.
- Having "organ donor" noted on your driver's license or carrying a donor card is all you have to do to become a donor.
- Only hearts, livers, and kidneys can be transplanted.
- A history of medical illness means organs or tissues are unfit for donation.
- Being too old prohibits organ donation.
- If you agree to donate your organs, your family will be charged for the cost.
- Organ donation disfigures the body and changes the way it looks in a casket.
- Religion prohibits organ donation.

Contraindications for Organ Donation

- Significant disease in the organ to be transplanted
- Significant mental dysfunction in donor and/or recipient
- Significant transmissible disease (HIV, sepsis)
- ABO blood type incompatibility
- Immunologic incompatibility
- High risk of perioperative morbidity and mortality
- Malignancy other than isolated CNS
- Extreme old or young age

Infections in Transplant Patients

TIME POST-TRANSPLANT	LIKELY SOURCE OF INFECTION
0-1 month	Post-surgical infection; UTIs (*Escherichia coli*), IV lines (*S. aureus*, *S. viridans*), wound infection (*S. viridans*), pneumonia (*S. pneumoniae*)
1-6 months	CMV, EBV, PCP, meningitis (Listeria), fungal sepsis
> 6 months	**Good graft function:** same as general population **Chronic infection with immune modulating viruses (i.e., hepatitis B/C):** ongoing end-organ damage **Chronic rejection:** acute and chronic opportunistic infections

Key:
UTI = urinary tract infection; CMV = cytomegalovirus; EBV = Epstein-Barr Virus; PCP = *Pneumocystis carinii* pneumonia

Cyclosporine Drug Interactions

INCREASES LEVEL	DECREASES LEVEL
Diltiazem	IV Trimethoprim sulfamethoxazole
Verapamil	Isoniazid
Nicardipine	Rifampin
Erythromycin	Phenytoin
Ticarcillin	Phenobarbital
Doxycycline	Carbamazepine
Fluconazole	Omeprazole
Ketoconazole	
Nafcillin	
Metoclopramide	
Alcohol	
FK506	

Most Common Diagnoses in Patients Requiring a Renal Transplant

Glomerular diseases	24%
Diabetes	20%
Hypertensive nephrosclerosis	14%
Polycystic kidney disease	9%
Tubular and interstitial diseases	5%

Causes of Late Post-Transplant Graft Dysfunction

- Obstruction
- Cyclosporine nephrotoxicity
- Other drug-related nephrotoxicity: ACE inhibitors, trimethoprim
- CMV infection
- Renal artery stenosis: uncommon, usually causes severe hypertension
- Recurrent primary disease, especially glomerulonephritis and metabolic disorders
- Hypertension
- Pyelonephritis
- Rejection

Most Common Infectious Causes of Death in Renal Transplant Recipients

- Pneumonia
- Sepsis
- Peritonitis
- Meningitis

Causes of Early (1-12 Week) Graft Dysfunction

- Acute rejection
- Cyclosporine nephrotoxicity
- Urinary tract obstruction
- Recurrence of primary renal disease
- Infection

Ultrasound Findings in Acute Rejection

- Increase in volume of the graft outside the normal range
- Enlarged and abnormally echo-poor pyramids that result in a more distinct cortico-medullary boundary
- Alternating echo-poor and echo-bright regions within the cortex due to hemorrhage or infarction
- Perirenal fluid collections

Etiology of Heart Failure in Transplant Patients

Coronary artery disease	45%
Dilated cardiomyopathy	46%
Valvular	3.5%
Retransplantation	2%
Congenital	2%
Miscellaneous	2%

Contraindications to Heart Transplant

- Advanced age (> 70 yr)
- Irreversible hepatic, renal, or pulmonary dysfunction
- Severe peripheral vascular disease or cerebrovascular disease
- Insulin-requiring diabetes mellitus with end-organ damage
- Active infection
- Recent cancer with uncertain status
- Psychiatric illness with poor medical compliance
- Systemic disease that significantly would limit survival or rehabilitation
- Pulmonary hypertension with increased pulmonary vascular resistance

Indications for Admission of a Heart Transplant Patient

- Congestive heart failure
- Fever
- Shortness of breath
- Hypoxia
- Poorly controlled hypertension
- New arrhythmia

Most Common Diagnoses In Patients Requiring Liver Transplant

- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Fulminant and subfulminant hepatitis
- Cirrhosis due to hepatitis B or C virus (most common)
- Alcoholic liver disease
- Biliary atresia and metabolic diseases
- Hepatocellular carcinoma

Contraindications for Liver Transplantation

- Extrahepatic malignancy
- Liver metastases
- Extrahepatic organ failure
- Noncompliance
- Active substance abuse
- AIDS
- Uncontrolled systemic infection

Targeted Physical Exam of the Organ Transplant Recipient

General: Vital signs (include orthostatic), volume status
Face: Periorbital edema (glomerulonephritis), sinus tenderness (sinusitis)
Ears: Otitis media or externa
Mouth: Thrush
Neck: Nuchal rigidity (meningitis, retropharyngeal abscess)
Lymphadenopathy: CMV, EBV, hepatitis
Skin: Rash (viral syndrome), jaundice, cellulitis
Lung: Pneumonia, pulmonary edema
Heart: Pericardial friction rub—virus, uremia
Abdomen: Peritonitis (often nonspecific), wound infection, localized tenderness
Rectal: Perirectal abscess
Extremities: Hemodialysis sites, central lines (bacteremia, cellulitis); peripheral edema (volume overload, venous thrombosis secondary to renal vein thrombosis)
Neurologic: Mental status, focal deficits

Contraindications to Pancreas Transplant

- Uncorrectable cardiovascular disease
- Active infection
- AIDS
- Malignancy within the past 3 years
- Active substance abuse
- Recent history of noncompliance
- Psychiatric illness
- Active untreated peptic ulcer disease
- Hepatitis B surface antigen positive
- Irreversible hepatic or pulmonary dysfunction

Indications for Admission in Liver Transplant Patients

- New onset graft failure
- Fever without obvious source less than one year post-transplant
- Fever in chronic rejection patient
- Persistent hypoglycemia

Supplement to *Emergency Medicine Reports*, January 12, 2004: "Evaluation and Management of Solid Organ Transplant Patients in the Emergency Department." *Authors:* **Lisa Freeman, MD, FACEP,** Assistant Professor, University of Texas Medical School at Houston, Department of Emergency Medicine; and **Sally Awad, MD, FACEP**, Assistant Professor, University of Texas Medical School at Houston, Department of Emergency Medicine.

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Volume 24 SUPPLEMENT

For a complete title index, please see page 16.

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Financial Disclosure Statement

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we present the following annual statement of disclosure for the editorial board members of *Emergency Medicine Reports.*

Paul S. Auerbach, MD; William Brady, MD; Kenneth H. Butler, DO; Michael L. Coates, MD; Alasdair K.T. Conn, MD; David A. Kramer, MD; Larry B. Mellick, MD; Paul E. Pepe, MD; Robert Powers, MD; Barry H. Rumack, MD; Richard Saluzzo, MD; David Sklar, MD; J. Stephan Stapczynski, MD; Charles E. Stewart, MD; Steven M. Winograd, MD; and Allan B. Wolfson, MD, report no relationships with companies related to the field of study covered by this CME program.

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Gideon Bosker, MD, editor-in-chief, is on the speaker's bureau for Pfizer, Rhone-Poulenc Rorer, and Parke-Davis. Dr. Bosker also acknowledges that he receives royalties, commissions, and other compensation relating to the sale of textbooks, reprints of articles, and other written materials to the following pharmaceutical companies: Pfizer, Genentech, Aventis, Pharmacia, and Bayer.

John A. Schriver, MD, and Corey M. Slovis, MD, did not return disclosure forms.

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