Medicine AND Health
RHODE ISLAND

Transplantation

What's in a Name???

GOOD - authentic, honest, just, kind, pleasant, skillful, valid

NEIGHBOR - friend, near

ALLIANCE - affiliation, association, marriage, relationship

CORPORATION - company, business establishment

A Good Partner Makes the Difference

It's Official:

The Rhode Island Medical Society's Insurance Brokerage Corporation

has contracted with

The Good Neighbor Alliance Corporation

to provide their members

Employee Benefits

Specializing in Employee Benefits since 1982

Let the Best in the Business Take Care of Your Employee Benefit Needs.

The Good Neighbor Alliance Corporation
1-800-462-1910 or 401-467-2880

www.goodneighborall.com

Cover: "After Life," 17-inch wooden box, composed of mixed media mish-mash of materials, by Melissa Ferreira, a Providence artist who teaches part-time in the Illustration Department at Rhode Island School of Design. "When not making commissioned pieces for clients, I create objects and images that interpret these spectacular human bodies of ours—inside and out—but in ways that resemble physiological models from the Middle Ages rather than the informed imaging we have today." www.melissaferreira.net.

Medicine ☙ Health
RHODE ISLAND

Commentaries

Summing Up

This is the 99th column that I've written for *Medicine & Health/Rhode Island*, and I hope to keep supplying them, one per month. It might seem that a summing up would be better suited for the 100th column, or when I retire from this position; however, I've always written an "April fool's" column, which will be the 100th, making a serious venture inopportune, and I'm not planning on stepping down from this position for a while yet. Since being editor-in-chief of this journal is not the most highly sought after position, it is unlikely that I will be forced from the job by an unexpected palace intrigue. What "palace?" What sort of an "intrigue?"

This journal is a small venture. It is sent to the thousand plus members of the RIMS and is given free to all Brown medical students. Some medical libraries subscribe, because they have contractual arrangements with other libraries in their collaborative "systems" to subscribe to all designated journals. The contents of our journal are included in Index Medicus and therefore in Pub Med, so all the articles show up in literature searches.

The journal's work is done almost entirely by the managing editor, Joan Retsinas, and myself. Stan Aronson, Brown Medical School's founding dean and editor-in-chief emeritus of this journal, writes a monthly column related to medicine in history, a half column on the etymology of medical terminology, and edits my columns. The editors are unpaid.

The journal is subsidized by the RIMS, the RI Department of Health, Brown Medical School and the RI Quality Partners. In a recent survey of RIMS members, the journal received a surprising recognition as being one of several aspects of the medical society that they liked. It is not clear if Brown medical students share that enthusiasm, as they've not been surveyed. Having taught Brown medical students for many years, I can state that no student ever asked me if I was the same Joseph Friedman who edits the medical journal. Nor has any student every quoted or asked about an article.

Aside from writing my column, what do I do? Mainly two things. The most important is to recruit guest editors. Most of our issues are devoted to single topics (e.g., autism, brain stimulation, atrial fibrillation, etc). I therefore need to think of topics that I believe will be of interest to most of our readers. I then try to find someone in the medical community who can pull together enough authors covering enough topics to make a full issue possible. I try, whenever possible, to highlight an area that Rhode Islanders excel in, but for which we may not be known. Sometimes a new service comes to Rhode Island but local doctors, unaware, continue sending their patients to Boston or elsewhere, not knowing that the service is readily available here. The authors are generally located in RI or have recently moved from Rhode Island and are collaborating with Rhode Islanders. Sometimes I ask someone to review recent advances, with reference to services available in RI, in a discipline, such as cardiology, urology or radiology.

We receive some unsolicited material, but not a lot. We encourage these. The journal is a good venue for fellows, residents and students to begin their publishing careers. Our turn-around time is unrivaled, and the chances for publication are higher than in national journals. When I began to edit the journal, Dr. Aronson, who had been editor for over ten prior years, told me that he would define me as successful when I was able to reject a submission as unworthy. That hurdle was crossed long ago. However, in the case of student and trainee submissions, we try to work with the authors to improve the article sufficiently to merit publication. Generally this is possible.

It may not seem so difficult to get this done. And generally it's not, but it is a never-ending surprise how often doctors will not return phone calls, e-mails or even letters. You'd think that as editor-in-chief of any journal, let alone the state journal of a very small place, I'd receive some "respect." But no. Even junior people ignore me. I used to think that bad manners in doctors was a uniquely Harvard quality, but Brown doctors, perhaps believing this is a desirable Ivy League tradition, confusing bad manners with eminence, seem to be emulating their more famous colleagues. I recently received several manuscripts from authors who clearly had never even scanned the journal and had no idea of what articles in the journal should look like, another form of disrespect. But for people who do read the journal it appears to be getting more favorable reviews. And the Medical Society is happy with its members' feedback.

We endeavor to "advertise" local activities. We have a policy of publishing book reviews of every book with a RI author, if the book is brought to our attention. Almost none have been. We welcome purveyors of new tests, new treatments or new ideas to write scholarly articles to educate the community, and make their own expertise known. We welcome letters to the editor. We have published few because we haven't received many.

Our goal is to keep our local doctors informed about what's going on in Rhode Island. We aim to encourage young doctors to make observations and then publish them. A scholarly medical group raises community standards. The trip to Boston is not too long, but it's not easy and parking's worse. Our goal is to help our community make that trip unnecessary.

– **Joseph H. Friedman, MD**

Euphemisms, Dysphemisms and Blasphemy

Politeness often impels us to choose a congenial synonym when a more accurate term, sometimes vulgar, might offend the listener. Thus we may perspire rather than sweat, call a funeral director a grief therapist, call a military retreat a tactical deployment or refer to a recently deceased individual as the dearly departed rather than one who has kicked the bucket, bought the farm or assumed room temperature.

The Greeks had a word for such a benevolent transformation: *euphemos*, meaning a good word; in English, euphemism. [And blasphemy to define its opposite.] The English language is now thoroughly saturated with relaxing, socially sanctioned phrases to temper the harshness of reality by employing circumlocution instead of brevity, clarity and directness. Given the generous plasticity of our language, unreality may now be cloaked in the guise of reality and madness with the aura of sanity. Graffiti, for example, has been called authentic, socially-relevant art, garbage dumps are referred to as sanitary landfills, nuclear bombs renamed as radiation enhancement devices and homeland residents are now called natives, indigenous nationals or aborigines, depending upon the degree to which they have been colonized.

Dysphemism, the antonym of euphemism, defines verbiage that is intentionally and unduly offensive rather than merely quaintly descriptive or quietly obfuscating. Dysphemic terms are particularly employed in sports journalism where, for example, the losing team may be annihilated, trounced or slaughtered but rarely just defeated.

Euphemisms, when consciously used to conceal the truth, are now called doublespeak as a silent homage to George Orwell's newspeak and doublethink. Nor is doublespeak confined to the vocabulary of used car salesmen [when used cars are called preowned vehicles] or real estate agents who now rename down payments as "initial investments" and "rural settings" to hide long driveways that require snow plowing in the winter.

Some euphemisms can bring humor into the choice of acceptable synonyms. Fishermen off the coast of New England have sometimes been call "cod fathers," a cowboy in the Midwest may jokingly be renamed as a "bovine attendant," those who steal books from college libraries are identified, in Freudian English, as "victims of bibliomania" and a botanical garden may be labeled as "plant parenthood."

Euphemisms are standard props in the language of government, the military, certainly newspaper columns and the domains of sex and bodily functions [it is a sad day for spontaneous love when foreplay is paraphrased as an "antecedent to interpersonal transaction."] The National Committee on Public Doublespeak, headed by Professor William Lambdin, has found such euphemisms as "escalated interpersonal altercation" for domestic murder, "plural relations" for the apartheid activities in South Africa, "personal flotation device" for a life-saver and "involuntarily leisured" for the unemployed.

In terms of governmental activities, for example, state murder is called "capital punishment" or "judicially sanctioned execution"; neither of these semantic alternatives, of course, lessens the end-result of the action. If, in reporting deaths due to military action, the word "kill" seems offensive, there are more benign substitutes such as "neutralize," "pacify," "victim of collateral action" or " one who is terminated with prejudice."

Many figures of speech modify the character and endurance of the message: such methods as irony, understatement, metaphor, allegory, hyperbole [often employed in advertising or as an inflation of job-titles], periphrasis, word deformation [substituting a modified word such as "darn" instead of "damn"] all in the interests of degrading truth as an option rather than a requirement.

Consider, for example, a recent story from the Maine Department of Health and Human Resources. During the 2000 – 2004 interval, there were 22,516 automobile accidents on the Maine roads involving feral animals; and 3,400 of these were motor vehicle collisions with moose. These collisions resulted in 1,583 injuries to humans and 17 deaths. The moose casualty rate, of course, was substantially higher. Most of these accidents took place after dark, particularly during the moose mating season of September and October.

The Maine Department of Motor Vehicles has recently undertaken a number of measures to lessen this problem. First, by clearing much of the underbrush lining the highways and thus improving driver vision, particularly at night. Second, by placing road signs where there have been frequent moose-vehicle collisions, under the presumption that either the drivers or the moose are literate. And third, by moose herd management. [The Department defines "herd management" as the increased issuance of moose-hunting permits, by state sanction, in those state areas with the highest frequencies of moose-vehicle collisions.]

It is comforting to know that the estimated 29,000 moose of Maine are not mindlessly slaughtered, savagely hunted down or indiscriminately struck by motor vehicles but are having their numbers scientifically diminished through "herd management." Mercy and the art of bureaucratic euphemisms are not dead.

– STANLEY M. ARONSON, MD
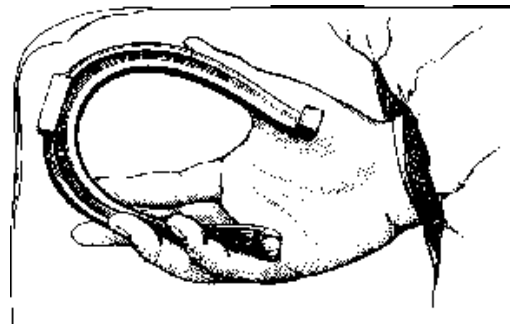
Solid Organ Transplation – Overview

Kevin Tan, MD, and Paul Morrissey, MD

Solid organ transplantation is the treatment of choice for many patients with end-stage organ failure from a wide variety of causes. This area of medicine has advanced over the last 50 years, improving patient survival and quality of life. The main problem today is not allograft rejection or infectious complications after transplantation, but the limited supply of organs that prohibits broader application of this therapy. (Figure 1, Table 1) Despite an ever-increasing number of transplants performed yearly, the waiting list outpaces the modest incremental improvements in deceased organ donation.

The **United Network for Organ Transplant (UNOS)** tracks transplantation statistics in the United States under contract from the federal government.[1] The **Organ Procurement and Transplantation Network (OPTN)** is the unified transplant network established by the United States Congress under the 1984 National Organ Transplant Act (NOTA), to be operated by a private, non-profit organization under federal contract. UNOS was awarded the OPTN contract to administer the OPTN under contract with the Health Resources and Services Administration of the **US Department of Health and Human Services (HHS)**. The primary goals of the OPTN are to (1) ensure the effectiveness, efficiency and equity of organ sharing and (2) increase the supply of donated organs available for transplantation. The national waiting list was 25% greater than the number of transplants recorded in 1988 and more than 50% greater by 1994. The tremendous clinical success of transplantation has created disparity in the number of patients waiting for transplantation and the availability of organs for transplant. In November 2006, there were over 93,000 listed candidates for organ transplant. UNOS's efforts to improve organ donation are discussed in a separate chapter in this issue.

ORGAN DONATION

The practice and terminology of organ donation have changed over the decades. The term "organ harvest" was replaced by "organ procurement" and most recently by "organ recovery." In the early days of transplantation asystolic deceased donors were the primary source of organs. The concept of brain death arose in 1968, first as a medical definition arrived at by a Harvard colloquium and later as the legal equivalent of death. Through the early 1990s brain dead donors were primarily standard criteria donors (young, previously healthy with good organ function). As the gap between the supply and demand for organs grew, the margins of acceptability were extended to include donors with reduced function and high-risk characteristics (prisoners, history of drug use, and history of cancer, e.g.); so called marginal and expanded criteria donors (older, depressed organ function). Recently there has been a re-emergence of cardiopulmonary arrested donors, referred to as **donation after cardiac death (DCD)**. Today these donors, all with severe irreversible brain injury, undergo end-of-life standard practices (extubation, discontinuation of IV fluids and vasopressors) with recovery of organs (usually kidneys and liver) after a five-minute documentation of cessation of cardiopulmonary function. At Rhode Island Hospital, 55 kidney transplants have been performed from DCD donors.

The vast majority of solid organs are procured from deceased donors with intact circulation and a clinical diagnosis of brain death. These donors have either died from traumatic brain injury, cerebrovascular accidents or secondary CNS injury (e.g., anoxia). Since 1988, the number of donors who died from motor vehicle collision or gunshot wound has steadily declined while the number of donors who died from primary central nervous events has increased.[2] The reasons for this include improved identifi-
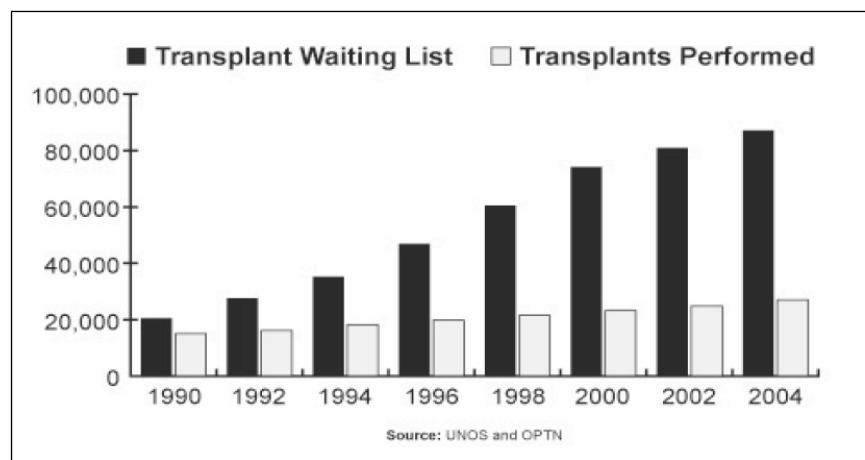
Figure 1. Solid Organ Transplantations Performed in the United States versus Growth of the Transplant Waiting List (all organs)

Table 1. Active Patients on the Transplant Waiting List by Organ Type

Organ	1996	1998	2000	2002	2004	Change from 1996-2004
Kidney	28775	34528	39989	44337	45676	158
SPK	1193	1480	2109	2062	1720	144
Liver	6285	9765	13927	13052	12744	203
Heart	2436	2525	2423	2055	1592	- 35
Lung	1718	2278	2485	2281	2167	126
Intestine	69	65	103	141	143	207

Source: 2005 OPTN/SRTR Annual Report

cation and referral of older donors, increased acceptance of older donors by transplant units, and improved automobile and handgun safety in the United States. There are in fact fewer young donors available than in years past rather than donors being overlooked or families refusing consent at higher rates limiting access to such donors.[3]

The transplant community in the United States has embraced living donation as a source of organs.[1] Worldwide practices vary greatly with nearly all kidneys transplanted in Japan and Korea coming from live donors, a distinct minority of kidneys from live donors in Europe and an increasing number of kidneys (now over 40%) of kidneys from living donors in the United States. In 2001, for the first time ever, the number of living donors in the United States (6607) exceeded the number of deceased donors (6100). Living donors may be related or unrelated to the recipient. Unrelated donors include spouses, distant relatives, friends, co-workers and altruistic strangers. The number of organs procured from living donors has plateaued in recent years. Live donors primarily donate a kidney (6647 in 2004), but also include liver (323), partial lung (24) and infrequently intestine (6) or pancreas (2) donors.

Just over 40 % of transplanted kidneys nationwide come from living donors. Compared to deceased kidneys, kidneys from living donors demonstrate superior long-term outcomes. (Tables 2 and 3) The observation that the results for living unrelated kidney donors were equivalent to living-related (and more closely HLA matched) revolutionized the field. The most common living unrelated kidney donor is a spouse; more commonly a wife as men outnumber women with end-stage renal disease and women make up a disproportionate percentage of altruistic donors. Interestingly, this analysis showed that the rate of graft survival at 3 years was higher for kidneys from spousal donors than for deceased transplants (85% versus 70%) despite a greater degree of HLA mismatching. The improved function of kidneys from living unrelated donors compared with deceased donors is attributed to improved organ quality, reduced ischemia-reperfusion injury, the absence of systemic aberrations due to brain death and reduced

cold ischemic time. These data also proved that HLA matching is of minor significance. Indeed only five criteria are essential for successful live donor transplantation: (1) overall good health, (2) normal renal function, (3) ABO compatibility, (4) HLA (crossmatch) compatibility, and (5) a willing donor free of undue coercion. For further information potential donors may refer to http://www.lifespan.org/rih/services/transplant/donor/.

OUTCOMES OF TRANSPLANTS

Initially patient survival was poor; however there were few medical alternatives. The technology of dialysis was rudimentary, and most patients faired poorly. The early experience with cardiac transplantation illustrates this point. Following the publicity of the first successful heart transplant in South Africa and the first successful heart transplant in the United States one month later under the direction of Norman Shumway at Stanford, surgeons performed 167 cardiac transplant procedures at 58 centers over the next two years. While the technical aspects of cardiac transplantation were within the capabilities of many surgeons, clinical and immunological as-

pects of patient care were poorly understood; and most patients died within a few weeks of surgery. The initial enthusiasm of the cardiac surgery community was tempered by the familiar nemeses of transplantation - rejection and infection. In the ensuing decade approximately 20-30 heart transplant operations were performed annually, one-third of them at Stanford University. Long-term survivors were rare. Only 35% of cardiac transplant recipients survived 3 months.[4] This changed with the introduction of cyclosporine in the early 1980s. The greater specificity of this agent controlled acute rejection with fewer morbid side effects than prednisone. Favorable results were rapidly achieved for kidney, liver, heart and pancreas transplantation. Both short term and long term survival rates improved. According to the 2005 OPTN/SRTR report, one-year survival was highest for kidneys and pancreas recipients, which ranged from 94.6 to 97.9%. One-year and five-year survivals are impressively high. (Tables 2 and 3)

Graft survival rates are generally lower than patient survival rates because patients may receive a second transplant or be supported by an alternative therapy

Table 2. Unadjusted One- and Five-Year Patient Survival (percent)

Organ Transplanted	1-Year Survival	5-Year Survival
Kidney (deceased donor)	94.6	81.1
Kidney (living donor)	97.9	90.2
Kidney-pancreas	95.3	85.9
Liver	86.8	73.1
Heart	87.5	72.8
Lung	83.0	49.3
Intestine	85.7	53.5

Source: 2005 OPTN/SRTR Annual Report

Table 3. Unadjusted One- and Five-Year Graft Survival (percent)

Organ Transplanted	1-Year Survival	5-Year Survival
Kidney (deceased donor)	89.0	66.7
Kidney (living donor)	95.1	80.2
Kidney-pancreas	91.7	76.5
Liver	82.2	66.9
Heart	86.8	71.8
Lung	81.4	47.5
Intestine	73.8	37.6

Source: 2005 OPTN/SRTR Annual Report

(dialysis). Of note, five-year patient survival is considerably better than allograft survival for kidney recipients, highlighting two important points: first, in the event of loss of allograft function patients may return to dialysis; second, one-half of all allografts are lost to chronic allograft nephropathy (formerly termed chronic rejection) with the recipient considerably outliving the functional allograft. Notably, 15% of the patients waiting for a kidney transplant have already lost one previous kidney. Kidneys transplanted from a live donor source result in superior long-term function. (Table 3)

KIDNEY TRANSPLANTATION

Transplantation is the treatment of choice for patient with **end-stage renal disease** (ESRD), providing longer survival, superior quality of life and reduced medical expenses compared with dialysis. There are very few absolute contraindications to kidney transplant, therefore most patients younger than age 60 and many under the age of 70 with ESRD should be considered for transplant evaluation. Nevertheless, only one of every six patients with ESRD is on the waiting list for a kidney transplant. Most are excluded because of advanced age and prohibitive co-morbid medical conditions. The survival advantage after transplant compared with continued dialysis has been shown for all age groups and all causes of ESRD; the greatest advantage is for diabetic patients.[5] Allograft survival for deceased donor and living donor transplants averages 65 and 80% at 5 years and 45 and 65% at 10 years, respectively.

PANCREAS TRANSPLANTATION

Successful pancreas transplant results in insulin independence and euglycemia, as well as the halt of progression in diabetic retinopathy, neuropathy and notable improvements in gastroparesis. Most importantly, pancreas transplantation substantially enhances the patient's quality of life and obviates the need for glucose monitoring and insulin administration. In accomplishing euglycemia, pancreas transplantation becomes the optimal therapy for diabetic, ESRD patients with hypoglycemic unawareness.

The major drawback for pancreas transplant is the need for immunosuppression, considered by most an unacceptable trade-off with the need for chronic insulin therapy. Therefore, pancreas transplantation is performed in diabetic patients with kidney failure who are candidates for a kidney transplant and will require immunosuppressive drug to prevent kidney rejection. The options for pancreas transplant are (1) deceased donor, simultaneous pancreas-kidney transplant (SPK), (2) living donor kidney transplant, followed by a deceased donor pancreas transplant and far less commonly (3) a **pancreas transplant alone** (PTA).

> ...15% of the patients waiting for a kidney transplanted have already lost one previous kidney.

LIVER TRANSPLANT

Liver transplant is the treatment of choice for patient with acute fulminant and chronic liver failure. Patient survival at one year posttransplant has increased from 30% in the early 1980s to more than 80% at present. This has led to an increase in number of liver transplants performed (approximately 2000 in 1990, 4000 in 1997 and over 6000 last year). In 2005, 6443 liver transplants were performed among over 16,000 people on the waiting list. Most of this growth was achieved through the more aggressive pursuit and recovery of deceased donor organs with a lesser contribution (about 5%) from living donors. Live liver donors include left lateral segmentectomy in parent-to-child transplantation and right hepatectomy for **adult-to-adult liver transplantation** (AALT). The donor mortality for AALT (0.5-1.0 %) introduced appropriate caution in adopting this procedure; there were 519 living liver segment donors in 2001, however there have been only 330 on average in the past five years.[2]

The leading indication for liver transplant is cirrhosis caused by non-cholestatic liver disease, primarily due to chronic **hepatitis C virus** (HCV) and al-cohol. The proportion of active patients on the waiting list with non-cholestatic chronic liver disease has been increasing. In 1995, 65% of patients waiting for liver transplantation had cirrhosis secondary to a non-cholestatic liver disease. In 2004, this had increased to 72% primarily driven by patients with HCV (40% of all listed patients). In 2004, cholestatic liver disease (sclerosing cholangitis, primary biliary cirrhosis), acute hepatic necrosis, biliary atresia, and metabolic liver disorders accounted for 11%, 4.5%, 1.7%, and 1.5% of patients on the active liver transplant waiting list, respectively.

In the United States there are over 120 centers performing liver transplantation, including eight in New England (Hartford Hospital, UMMC, Yale, Lahey and four centers in Boston). Approximately 8-12 people from Rhode Island receive a liver transplant each year. Given the proximity to other centers our administrators and we have not pursued liver transplantation at Rhode Island Hospital. Such a pursuit would require enormous resources including more ICU beds, specialists in hepatology and pathology and dedicated teams in anesthesiology and nursing. It appears that the number of liver transplants would be insufficient to maintain satisfactory skills for optimal transplant care.

THORACIC ORGAN TRANSPLANTATION

Heart transplantation is generally performed in patients with life expectancy less than one year. From 1995 to 2004, the number of patients on the heart waiting list declined, primarily a reflection of the decline in the percentage of transplant candidates with a coronary artery disease classification. This may reflect better outcomes resulting from improvements in medical, interventional, and surgical treatments for coronary disease. The number of heart donors has remained stable over recent years, with approximately 2000-2200 heart transplants performed annually, of which 20% are in children. The most common cause is ischemic or dilated cardiomyopathy, follow by valvular disease and congenital heart disease. Lung transplantation is newer field than heart transplantation. Currently, **chronic obstructive pulmonary disease** (COPD) is the most com-

mon indication, followed by pulmonary fibrosis, cystic fibrosis, primary pulmonary hypertension and alpha-1 antitrypsin deficiency. There are three major approaches: single-lung, bilateral sequential lung transplant and transplantation of lobes from living donors (less than 25 cases annually). For six consecutive years, the number of patients on the active waiting list for a heart-lung transplant has decreased, from a high of 179 patients in 1998 to only 83 in 2004. Most waiting list patients for heart-lung transplantation (81%) were adults older than 18 years. The most common diagnoses were congenital heart disease (35%), primary pulmonary hypertension (18%), and cystic fibrosis.

INTESTINAL TRANSPLANT

Intestinal transplantation is the least frequently performed solid organ transplant and associated with the highest rejection rates and lowest graft survival. It is reserved for patient with poor intestinal function who cannot be maintained on **parenteral nutrition (TPN),** or those with TPN-associated complications, including hepatic dysfunction. There is evidence that the majority of patients with progressive organ failure are referred to transplant centers at a later stage of their disease. As a result the Clinical Practice Committee of the American Society of Transplantation has made the following recommendations: (1) early referral to a transplant center for patients with organ insufficiency, (2) close cooperation with the primary care doctor regarding follow-up and appropriate referral to the transplant center with disease progression and (3) regular communication about any changes in the condition of patient that affect eligibility for transplantation.[6]

Transplantation of the intestine, either isolated or in combination with other abdominal organs, is being performed with increasing success. The number of patients who received a small intestine transplant has gradually increased over the past 10 years from 46 in 1995 to 152 in 2004. In 2004, 443 patients were alive with a functioning intestine graft. These numbers point to the need for highly specialized care for these complex patients.

THE ECONOMICS OF TRANSPLANTATION

Funding sources for organ transplantation include private health insurance, Medicare, Medicaid and the Veterans Administration system. Additional funding is available through charitable organizations, advocacy groups, and prescription drug assistance programs. The latter includes programs established by private drug companies and a variety of state-funded initiatives. Residents of Rhode Island for at least one year prior to the date of the transplant operation and with a household income less than $66,309.82 are eligible for monies through the Rhode Island Organ Transplant Fund. After the recipient's insurer has made payment, any remaining costs are considered for reimbursement.

Organ transplantation costs, on average, $250,000 for liver, $150,000 for heart and $80,000 for kidney (deceased or live donor). Obtaining health insurance is a prerequisite for patients with organ failure. Insurance coverage is not available to undocumented aliens and organ transplantation is denied unless the individual can cover the cost of transplantation or the money is raised thorough charitable appeals.

Kidney transplantation is more cost-effective than hemodialysis for the Medicare program. The initially higher costs of transplantation are fully recouped by Medicare within three years after surgery. Unfortunately, Medicare coverage for immunosuppressants ends 36 months after transplantation. At that time patients must obtain private insurance, qualify for Medicaid or enter patient assistance programs to obtain funds for transplant immunosuppression; the yearly cost ranges from $2000 – $12,000.

The Medicaid Program requires states to cover "categorically needy individuals," which typically includes low-income families with children and pregnant women. A second category, Medically Needy, allows one to subtract medical expenses from income. A "spend down" is the process of using medical expenses to reduce income to the level that qualifies for Medicaid. Through these mechanisms the majority of people with end-stage organ failure obtain coverage for transplantation.

CONCLUSION

This overview demonstrates that the field of transplantation continues to improve as a surgical (technical) and medical discipline. Improvements in the pre- and post-transplant care of patients with organ failure and the continued progress in immunosuppression make this one of the most exciting areas in clinical medicine. Undoubtedly, improvements will continue in this "new" field, which celebrated its 50th anniversary in 2004.[7]

REFERENCES

1. Organ Procurement and Transplantation Network. www.optn.org. Accessed November 20, 2006.
2. 2005 OPTN/SRTR report. www.ustransplant.org. Accessed November 20, 2006.
3. Hauptman PJ, O'Connor KJ. Procurement and allocation of solid organs for transplantation. *NEJM* 1997; 336: 422.
4. Pennock JL, Oyer PE, et al. Cardiac transplantation in perspective for the future. *J Thorac Cardiovasc Surg* 1982; 83:168.
5. Wolfe RA, Ashby VB, et al. Comparison of mortality in all patients on dialysis. *NEJM* 1999; 341: 1725.
6. Guidelines for referral and management of patients eligible for solid organ transplantation. *Transplantation* 2001; 71: 1189.
7. Sayegh MH, Carpenter CB. Transplantation 50 years later—progress, challenges, and promises. *NEJM* 2004; 351: 2761.

Kevin Tan, MD, is a resident in surgery, Rhode Island Hospital.

Paul Morrissey, MD, is Associate Professor of Surgery, Brown Medical School, and Division of Organ Transplantation, Rhode Island Hospital.

CORRESPONDENCE:

Paul Morrissey, MD
Rhode Island Hospital APC 921
593 Eddy Street
Providence RI 02903
phone: 401-444-5285
E-mail: pmorrissey@lifespan.org

Transplantation at Rhode Island Hospital:
A Decade of Commitment

Paul Morrissey, MD

Kidney transplantation for residents of Rhode Island has a long and interesting history. After training at the Peter Bent Brigham, Joseph Chazan, MD, opened the first dialysis unit in Rhode Island in 1970. The unit was established at the Rhode Island Hospital and shortly thereafter the first freestanding unit was opened in the "six corners" location in East Providence. Shortly thereafter a transplant unit was established at the Miriam Hospital. Robert Hopkins performed six kidney transplants between 1973 and 1975. The program closed thereafter. For the next 21 years patients were referred to transplant centers in Boston and Connecticut for transplantation. Tony Monaco, MD, at the New England Deaconess Hospital, transplanted the majority of Rhode Islanders with end-stage renal disease. With the encouragement of Joseph Chazan in the community and the assistance of Peter King, MD, Lance Dworkin, MD, and Kirby Bland, MD, then Chief of Surgery, a transplant program was established at the Rhode Island Hospital in 1996. The program was first a satellite of the NEDH with Reg Gohh, MD, serving as medical director and Bette Hopkins, RN, as Transplant Coordinator. Pre- and post-transplant patients from Rhode Island were cared for at the clinic. In March 1997, the first transplants were performed from a deceased donor in Rhode Island; in June the first living related transplant was undertaken. I joined the program at that time and since then we have expanded to include specialists in infectious disease, psychiatry, social work, pharmacology, nutrition and research programs. Since 2004, the Transplant Team includes 9 physicians, 5 nurses, 7 allied health care professionals and 5 office assistants. Transplant volume is shown in Figure 1.

ORGAN DONATION AND THE LOCAL WAITING LIST

As the only Level 1 Trauma Center in the state, Rhode Island Hospital is the predominant site for deceased organ donation. In the past 10 years, 239 kidneys were recovered at Rhode Island Hospital, compared with 14 at Kent, 8 at Roger Williams and 4 each at Miriam and Newport Hospitals. These stark differences are related to differing patient populations with conditions that result in organ donor potential – trauma, cerebrovascular accidents and other causes of irreversible brain injury or brain death. The majority of kidneys recovered in Rhode Island are transplanted within the state as allocation in New England is heavily biased toward geography. Rhode Island Hospital is consistently a leader in deceased organ donation in the region. (Table 1) Our surgical group is assigned primary responsibility for kidney recovery throughout Rhode Island; often we also recover the liver and pancreas for use within the region or nationally. Rhode Island Hospital was the fourth center in New England to adopt a policy for donation after cardiac death (kidney recovery after withdrawal of mechanical ventilation in patients with devastating head injury) and such donors have provided a valuable source of kidneys (n=63) for transplantation.

Just over 45 % (296/640) of transplanted kidneys at Rhode Island Hospital come from living donors. Most are from relatives. The most common living unrelated kidney donor is a friend (n=35), followed by a spouse or fiancé (34); more commonly a wife (22) as men outnumber women with end-stage renal disease and women always make up a disproportionate percentage of living donors. In 1999, our program became one of the first in the country to accept a stranger (nondirected, altruistic) donor. We now boast, on behalf of our generous donors, the second largest reported series of Good Samaritan and nondirected donors (22) in the United States. [1] The University of Minnesota has the most (around 40).

With these strong efforts in living and deceased donor organ donation, the latter elaborated in greater detail by Kevin Dushay, MD, in an accompanying article, the wait-list for kidney transplantation in Rhode Island is shorter than at Yale and the Boston programs. Even so, we have a crucial need. Rhode Island patients on the active UNOS wait list include: kidney (128), pancreas (22), liver (92), heart (18) and lung (12).

Figure 1. Live donor renal transplants (LDRT) and total kidney transplants at Rhode Island Hospital, by year
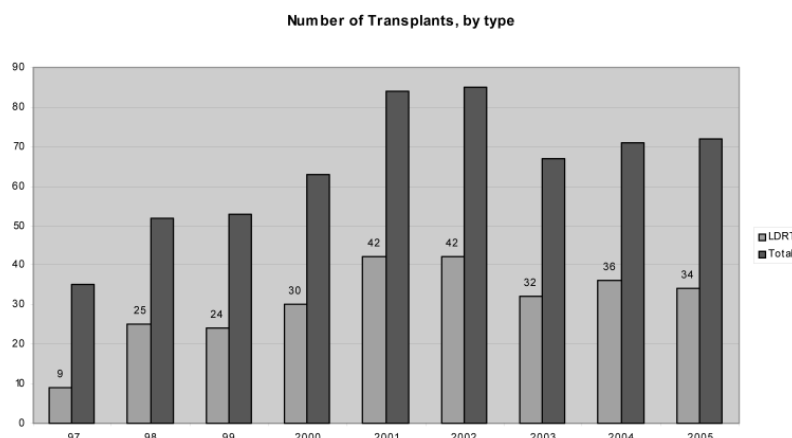
Table 1. Top kidney transplant centers by volume in New England, 1997-2006	
Transplant Center	**Renal Transplants**
Yale-New Haven	324
Rhode Island Hospital	315
Maine Medical Center	310
BIDMC	310
MGH	302
Brigham & Women's	217
NEMC	205
Univ. of Massachusetts	185
Source: 2006 New England Organ Bank Report	

Table 2. Unadjusted Patient and Allograft Survival (percent) at Rhode Island Hospital		
Kidney Recipients	**Patient Survival**	**Allograft Survival**
One-year	93	89
Two-year	91	84
Three-year	89	81
Five-year	84	69
Source: RIH data		

KIDNEY TRANSPLANTATION

Transplantation is the treatment of choice for patients with **end-stage renal disease (ESRD)**, providing better patient survival, superior quality of life and reduced medical expenses compared with dialysis. There are very few absolute contraindications to kidney transplant, therefore most patients younger than age 60 and many under the age of 70 with ESRD should be considered for transplant evaluation. In fact, only one of every six patients with ESRD is on the waiting list for a kidney transplant (153 patients of 950 on chronic dialysis in Rhode Island). Most are excluded because of advanced age and prohibitive co-morbid conditions.

Kidney allograft survival rates are lower than patient survival as recipients with a failed kidney allograft may receive a second transplant or return to dialysis. Our overall patient and graft survival is shown in Table 2. The majority of deaths were due to sepsis and cardiovascular causes, particularly in the subgroup of older recipients.[2] Additional allograft losses were due to chronic allograft nephropathy, infection (BK virus, e.g.), and allograft rejection often related to medication nonadherence. This occurrence, whether related to psychological illness, economic hardships or immaturity, is an unfortunate consequence of the need for chronic immunosuppression.[3]

PANCREAS TRANSPLANTATION

Successful pancreas transplant results in insulin independence and substantially enhances the patient's quality of life. Therefore, pancreas transplantation is the optimal therapy for diabetic, ESRD patients with hypoglycemic unawareness. For many patients with diabetes and renal failure the opportunity for deceased donor kidney-pancreas will provide optimal survival and quality of life.[4]

The options for pancreas transplant are deceased donor, **simultaneous pancreas-kidney transplant (SPK)** and living donor kidney transplant; followed by deceased donor pancreas transplant—**pancreas after kidney (PAK)** transplantation. To date, 24 patients with ESRD and diabetes have received a pancreas transplant (19 PAK, 5 SPK) since 2002. With a mean follow-up of 30 months, 23 patients are alive with a functioning kidney and 15 (62%) are insulin-free. As islet cell transplantation, xenotransplantation and optimal insulin pump technologies continue to require refinement, pancreas transplantation for patients with diabetes who already require immunosuppression for a kidney allograft remains an appealing option.

REFERENCES

1. Morrissey PE, Dube C, et al. Good Samaritan kidney donation. *Transplantation* 2005; 80: 1369.
2. Morrissey PE, Yango A. Renal transplantation: older recipients and donors. *Clin Geriatr Med* 2006; 22: 687.
3. Morrissey PE, Flynn M, Lin S. Medication non-compliance and its implications in transplant recipients. *Drugs* 2007; in press.
4. Reddy KS, Stablein D, et al. Long-term survival following simultaneous kidney-pancreas transplantation versus kidney transplantation alone in patients with type 1 diabetes mellitus and renal failure. *Am J Kidney Dis* 2003; 41: 464.

Paul Morrissey, MD, is Associate Professor of Surgery, Brown Medical School, and Division of Organ Transplantation, Rhode Island Hospital.

CORRESPONDENCE:

Paul Morrissey, MD
Rhode Island Hospital APC 921
593 Eddy Street
Providence RI 02903
Phone: (401)
E-mail: pmorrissey@lifespan.org
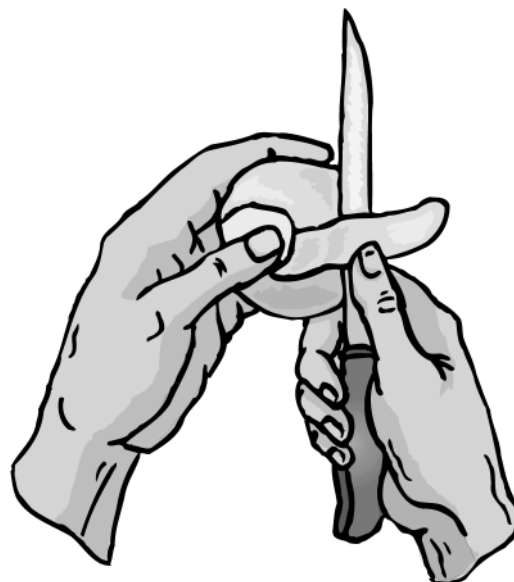
Pediatric Renal Transplantation –
Historic and Current Perspectives

M. Khurram Faizan, MD, and Andrew S. Brem, MD

Renal transplantation is the preferred mode of therapy for pediatric patients with chronic kidney disease. Successful kidney transplantation offers children with **end stage renal disease (ESRD)** the opportunity for normalization of growth and development. Obstructive uropathy and associated renal dysplasia remain the commonest causes of ESRD in the pediatric age group.[1,2] According to the **United Network of Organ Sharing (UNOS)** database, approximately 700 pediatric renal transplants are performed each year. Since 1988, a total of 13,163 successful pediatric renal transplants have been carried out in the United States (www.unos.org).

Pediatric centers in Minnesota and California were the first to offer kidney transplantation to children with end stage renal failure in the late 1960s. Those pioneering pediatric nephrologists and transplant surgeons recognized that renal failure in children was a functional death sentence[3] since chronic dialysis was not readily available at that time. Immunosuppression was primitive, kidney donors were few, and medical insurance covering the expense was not always available. The Congressional passage of the Medicare End Stage Renal Disease entitlement program in 1973 fundamentally changed the dynamic by, at the least, guaranteeing payment for the transplant. Other pediatric centers soon began offering transplant services with the assurance that their expenses would be defrayed. Pediatric dialysis services also improved with Medicare funding, but chronic dialysis treatment could never fully compensate for the multiple medical and psychosocial problems associated with renal failure. Over the next twenty-five to thirty years, advances in immunosuppression, living donor transplantation, and changes in deceased donor organ allocation criteria have established kidney transplantation as the treatment of choice for children with chronic renal failure.

PEDIATRIC RENAL TRANSPLANTATION PROGRAM AT RHODE ISLAND HOSPITAL

The Rhode Island Hospital initiated its own kidney transplant program in 1997. Prior to that time, all adult and pediatric patients were required to travel out of state for renal transplantation. Our pediatric transplant program was launched in 1998 with an 11-year old boy receiving a kidney from his mother. Since then, 20 patients ranging from 2 to 18 years have received 21 renal transplants. (Table 1) Approximately 60% of these renal transplants were done with living donors. In contrast to adult experience, living donor transplants are more common than deceased donor transplants for pediatric patients.[4] Outcomes in our program have compared favorably to national data[4] with 100% patient survival and a one-year graft survival of 95%. The one loss was due to recurrent disease (focal segmental glomerulosclerosis), a known risk factor.[5] The relatively small numbers of pediatric transplants reflect the low incidence of ESRD in children - approximately 2 to 3 cases per million population.

UNIQUE ASPECTS OF PEDIATRIC END STAGE RENAL DISEASE AND RENAL TRANSPLANTATION

Children undergoing long-term dialysis face a multitude of problems. Chronic dialysis although life-saving, is not a panacea. Clearance of excess fluid and waste products by dialysis is cyclic and not the same for all toxins. Children on dialysis often have limited appetites especially given necessary dietary restrictions. With inadequate caloric intake, normal growth is unlikely. Ad-

Table 1. Rhode Island Hospital Experience with Pediatric Renal Transplantation

Patient	Age at transplant	Sex	Original Diagnosis	Creatinine (mg/dl) post transplant
1	17	m	congenital obstruction	1
2	11	m	congenital obstruction	0.6
3	17	f	SLE	0.8
4	9	f	FSGS	1.1
5	14	m	Vasculitis	1.3
6	17	f	crescentic GN	0.6
7	13	f	neonatal cortical necrosis	0.4
8	3	m	congenital obstruction	0.2
9	14	f	RPGN	0.8
10	14	m	renal dysplasia	1.1
11	17	m	PCKD	1.1
12	13	f	Vasculitis	0.7
13	17	m	congenital obstruction	1
14	17	f	Unknown	0.8
15	10	f	renal dysplasia	0.6
16	16	f	Vasculitis	1.4
17	2	m	PCKD	0.2
18	15	m	congenital obstruction	1.2
19	17	m	congenital obstruction	1.2
20	16	f	FSGS	0.9
21	16	m	SLE	0.8

SLE = Systemic Lupus Erthematosus, FSGS = Focal Segmental Glomerulosclerosis,
RPGN = Rapidly Progressive Glomerulonephritis, PCKD = Polycystic Kidney Disease.

ditionally, multiple medications are needed to augment the dialysis treatments including erythropoietin for control of anemia and calcium supplements with 1,25 (OH)2 vitamin D to ensure proper bone mineralization. From a psycho-social perspective, the time required to undergo hemodialysis, usually 3 to 4 hours for three sessions per week, imposes a heavy hardship on children removing them from the usual childhood activities of school and play. Working parents also have the burdens of transportation and caretaking. Families performing **peritoneal dialysis (PD)** at home must care for a sick child and deal with the infectious and nutritional complications of PD. Successful renal transplantation in children allows for restoration of growth and development, improvement in school performance and cognitive abilities, an increase in the physical activity level, and allows families to lead a more normal life with their children at home.

Parents are often ready and willing to serve as candidates for living donor transplantation when their own children are involved as patients. The **United Network for Organ Sharing** (UNOS) also has recognized the special needs of children with ESRD and favors allocating deceased donor organs to children under 18 years of age when possible. These two advantages increase organ availability and most children fortunately now spend a relatively brief time undergoing dialysis prior to transplantation. Currently, most transplant centers in the United States use an immunosuppressive regimen in pediatric patients that mimics their adult counterparts. However, a few centers have attempted to minimize the use of posttransplant steroids in children due to their negative effect on growth. Unfortunately, teenagers comprise the highest risk of acute transplant rejection amongst any age group (including both children and adults). This is due to a high rate of medical non-compliance seen in this age group.

Pediatric renal transplantation is a labor-intensive exercise with attendant pitfalls and potential complications. Kidneys from adult donors are preferred even for the youngest patients. This means that the patient needs appropri-ate volume expansion in the operating room to prevent hypo-perfusion and thrombosis. Young patients often metabolize immunosuppressive medications more quickly than adults and require close monitoring of drug levels in the post-operative period. Hypertension both from medications and/or from prior volume expansion is a frequently encountered problem. In the short-term, we accept higher blood pressures in transplant patients as long as they are asymptomatic to avoid the risk of thrombosis in the graft. The risk of infection is ever present in children post-transplant; the infections come from outside exposures or can be inadvertently acquired from the donor in the transplant process.

> **Most pediatric patients do very well in the United States with a five-year graft survival of about 82% and a five-year patient survival of 92%.**

More mundane issues surface in our patients as time passes. Immunizations often have been deferred and need to be considered. As a rule, most transplant centers, including our own, do not recommend giving attenuated live virus vaccines to patients. Patients frequently are concerned about their delayed linear growth, which resulted from prior renal failure. Fortunately, newer immune-modulating protocols now limit glucocorticoid exposure[6] and many children will resume a normal growth velocity or even exhibit "catch up" growth after transplant. We encourage patients to begin regular exercise once their wounds are healed. Regular exercise for as little as 30 minutes a day helps patients lower their risk for hypertension, excessive weight gain, and diabetes post transplant.

CONCLUSIONS

Active participation and cooperation of the parents are necessary to ensure that children receive prescribed drugs regu-larly and maintain clinical follow-up after transplantation. A multi-disciplinary approach is essential, with the pediatric renal transplant team comprising of transplant surgeons, pediatric nephrologists, social workers, transplant coordinators, nurses and counselors to ensure a successful outcome post-transplant. Most pediatric patients do very well in the United States with a five-year graft survival of about 82% and a five-year patient survival of 92%.

REFERENCES

1. Lewy JE. Treatment of children in the U.S. with end-stage renal disease (ESRD). *Med Arch* 2001; 55:201-2.
2. Seikaly MG, Ho PL, et al. Chronic renal insufficiency in children. *Pediatr Nephrol* 2003; 18:796-804. Epub 2003 Jun 14.
3. McDonald SP, Craig JC. Long-term survival of children with end-stage renal disease. *NEJM* 2004; 350:2654-62.
4. Long-term graft survival in pediatric renal transplant patients based upon primary disease. *Transplantation* 2006; 82:100.
5. Baum MA, Ho M, et al. Outcome of renal transplantation in adolescents with focal segmental glomerulosclerosis. *Pediatr Transplant* 2002; 6:488-92.
6. Halloran PF. Immunosuppressive drugs for kidney transplantation. *NEJM* 2004; 351:2715-29.

M. Khurram Faizan, MD, is Clinical Assistant Professor of Pediatrics, Brown Medical School.

Andrew S. Brem, MD, is Professor of Pediatrics, Brown Medical School.

CORRESPONDENCE

M. Khurram Faizan, MD
Section of Pediatric Nephrology
Rhode Island Hospital APC 942
593 Eddy Street
Providence RI 02903
phone: (401) 444-5672
e-mail: Mfaizan@lifespan.org

Immunosuppression Strategies in Kidney Transplantation

Angelito Yango, MD, and Amit Johnsingh, MD

The development of immunosuppressive drugs heralded new and exciting possibilities in kidney transplantation. More than half a century ago, initial attempts at kidney transplantation resulted in immunologic destruction of the graft within a few weeks and eventual death of the recipient from renal failure, leaving little hope for optimism. Such sentiment changed, however, with the successful non-twin kidney transplantation in the late 1950s at the Peter Bent Brigham Hospital.[1] Previously the Brigham team and groups in France had performed successful kidney transplants among identical twins. Overcoming immunologic barriers between genetically dissimilar individuals by immunosuppression, however, ranks as this group's greatest achievement.

Equipped with the knowledge that rejection was an immunologic phenomenon, efforts were taken to weaken the immune system. Prior to the publication of acquired tolerance, Medawar and others reported on the immunosuppressive effects of total body irradiation and of the newly **synthesized hormone coricosteroids**. In 1952, Frank Dixon reported in the *Journal of Immunology* that x-rays could depress immune responsiveness. The first use of clinical immunosuppression was at the Peter Bent Brigham Hospital (1958 - 1960), using total body irradiation with subsequent reconstitution by a bone marrow allograft. Protocols were derived from experimental studies conducted by Joseph Murray and others in skin grafted rabbits. It was suggested that by infusing donor specific lymphoid cells into a recipient depleted of its own lymphocyte by irradiation, one might create a "chimeric" subject tolerant of organs and tissues from the donor of the allogeneic marrow. The initial cases were associated with short-term success and a high rate of complications related to the transplant operation, renal failure or bone marrow suppression. One patient with profound thrombocytopenia succumbed to bleeding complications one month after renal transplantation. Two postoperative biopsies and the kidney at autopsy failed to demonstrate any evidence of rejection. In the group's sixth case, the protocol was modified for a living related renal transplant from a fraternal twin. A lack of identity was clinically apparent and immunologic disparity was proven by preoperative and postoperative skin grafts that were rapidly rejected. Given the closeness of the relation, 450 Gray of total body irradiation, a reduction from earlier transplants, was administered eight days preoperatively. The allograft was accepted representing the first successful living related renal transplant under immunosuppression.[1] French surgeons soon replicated the successful protocol, first in the identical setting of living related renal fraternal twins and a year later in a sister-to-brother

The next major breakthrough occurred with the identification of potent immunosuppression from a product of a soil fungus identified in the Arctic Circle.

combination. Several other long-term successes were reported with protocols with total body irradiation; and Jean Hamburger, founding president of the International Society of Nephrology, showed that further radiation could reverse acute rejection in the allograft. This strategy was soon widely applied at Denver, UCLA, University of Minnesota, Edinburgh, Hammersmith, the Massachusetts General Hospital and the Medical College of Virginia. The following year, a second strategy in clinical immunosuppression arose from the development of 6-mercaptopurine in the laboratory. Subsequently, azathioprine was developed in collaboration with clinicians interested in transplantation and applied to the clinical arena after careful experiments in animal models conducted by Sir Roy Calne while a visiting fellow in the laboratory of Joseph Murray.

Significant progress has been made in surgical techniques as well as medical management of renal transplant recipients. Advances in transplant immunology paved the way for the development of immunosuppressive agents that are integral to successful allograft function. With the use of azathioprine and corticosteroids in combination, the average 1-year graft survival was less than 35%. This improved to 50% with the use of polyclonal antibodies that were produced in laboratories and animal facilities associated with the individual transplant centers. The next major breakthrough occurred with the identification of potent immunosuppression from a product of a soil fungus identified in the Arctic Circle. This compound, cyclosporine A, was originally purified in an effort to identify antifungal medications by Sandoz Laboratories in Basel Switzerland. Cyclosporine, it turns out, had weak antifungal properties, but was fortuitously noted to suppress immune function in a hemagglutinin assay. This wonderful agent may have been lost to clinical medicine had it not been for the self-experimentation of Jean Borel and H. Stahelin. The oral bioavailability of this endecapeptide was so poor that its immunosuppressive properties were lost *in vivo*. However, by dissolving the compound in oil prior to ingestion the scientists were able to detect significantly greater levels in their serum. Roy Calne, now at Cambridge, took the compound to the transplant laboratory and then to the clinic and proved its efficacy as an immunosuppressive agent.[2] Refinements in clinical immunosuppression with the combination of cyclosporine, azathioprine and prednisone set the stage for modern immunosuppression with 1-year allograft survival approaching 80%. The current state of the art immunosuppression regimens have now achieved 1-year patient and graft survival rates of greater than 95% and 88%, respectively.

In this brief review we will focus on current immunosuppressive regimens in

Table 1. Immunosuppressive Drugs Currently Used in Kidney Transplantation

Class	Drug	Comment
Depleting antibodies	Thymoglobulin (rabbit ATG)	Polyclonal Abs to T cells
	Muromonab-CD3 (OKT3)	mAb against CD3 (pan T cell)
	Alemtuzumab (Campath)	mAb against CD52
Nondepleting Ab	Daclizumab (Zenapax)	Anti-CD25 (IL-2 receptor)
	Basiliximab (Simulect)	Chimeric anti-CD25
Calcineurin Inhibitors	Cyclosporine (Neoral)	Inhibits cytokine (IL-2) production
	Tacrolimus ((Prograf)	Similar to CsA
Antiproliferative agents	Azathioprine (Imuran)	
	Mycophenolate mofetil (MMF, Myfortic)	Improved lymphocyte specificity synthesis
	Sirolimus (Rapamune)	Blocks IL-2 receptor signal
Corticosteroids	Methylprednisolone	Lymphocyte depletion in high doses
	Prednisone	Nonspecific cytokine reduction

use as well as evolving strategies and regimens in renal transplantation.

In general, allograft rejection is mediated by activated T lymphocytes, which infiltrate the graft leading to inflammation and eventual destruction. The best immunosuppressive drugs target T cell activation, cytokine production and proliferation. This is achieved by combining two to three drugs that act at different stages of T cell activation. Following kidney transplantation, immunosuppression is typically administered in three distinct phases.

INDUCTION IMMUNOSUPPRESSION

This phase involves intense immunosuppression in the immediate post transplant period when the risk of acute rejection is at its highest. Typically, standard immunosuppressive drugs used in the maintenance phase are also given at higher doses. For patients at high risk for rejection, such as those who are highly sensitized or have had previous organ transplants, the immunosuppression may be further intensified by the administration of anti-T cell antibodies. These antibodies act by binding to specific lymphocyte cell surface receptors causing lymphocyte depletion by way of phagocytosis or complement-mediated cell lysis.

T cell depleting antibodies include the polyclonal antilymphocyte antibodies – **equine ATGAM** (Pharmacia) and **rabbit ATG** (Thymoglobulin, Genzyme) and the monoclonal antibodies **OKT3** (Ortho Pharmaceutical) and **Alemtuzumab** (Campath, Genzyme).

Currently, Thymoglobulin is the preferred agent for induction, being superior to ATGAM in reversing acute rejection.[3] The use of anti T-cell antibody preparations does come with a price. It is associated with profound and prolonged lymphopenia risking serious opportunistic infections, bone marrow suppression and malignancy. Therefore, induction therapy should be reserved for patients at high risk of acute rejection or administered as a strategy to reduce maintenance immunosuppression.

For patients who are at low risk for early acute rejection, such as the elderly and unsensitized first-time recipients, one may elect to withhold induction therapy. Alternatively, one may use a nondepleting antibody that is specific only to activated T-lymphocytes. The prototypes for this class of agents are **basiliximab** (Simulect, Novartis) and **daclizumab** (Zenapax, Roche), which block interleukin-2 receptors expressed in activated T-cells. Since these drugs do not affect resting T cells, they do not deplete T cells and have minimal side effects.

MAINTENANCE IMMUNOSUPPRESSION

Following the initial phase of avid immunosuppression, patients begin a maintenance regimen to prevent late allograft rejection. Over the last decade, transplant immunosuppressive therapy has focused on T-cell specific immunosuppression including tacrolimus, mycophenolate mofetil and sirolimus; each proven more efficacious than the nonspecific agents azathioprine and prednisone. In the maintenance phase different classes of immunosuppressive agents are prescribed to target different stages in T cell activation. The major combination used in most centers, including ours, is a calcineurin inhibitor (cyclosporine or tacrolimus) augmented by an antiproliferative agent (azathioprine or mycophenolate mofetil) and corticosteroids. (Table 1)

Calcineurin inhibitors (cyclosporine or tacrolimus) remain the cornerstone of immunosuppression in renal transplantation. They act by inhibiting calcineurin, a key enzyme in T cell activation. **Cyclosporine** (CsA; Neoral; Sandimmune; Novartis) was first introduced in the 1980s and brought about significant reduction in acute rejection rates and dramatic improvement in one year cadaveric graft survival rates from 50% to 80%. In 1999, **Tacrolimus** (Prograf; Astellas), a macrolide antibiotic was approved for kidney transplantation and was shown in large multicenter trials to be superior to cyclosporine in preventing acute rejection.[4] By 2004 tacrolimus was the calcineurin inhibitor used by 80% of kidney transplant recipients.

Because the mechanism of action is similar, cyclosporine and tacrolimus cannot be used synergistically. In addition, while both drugs are equally nephrotoxic, their side effect profiles are distinct from one another. For example, tacrolimus is more neurotoxic and likely to induce post transplant diabetes. On the other hand, compared to cyclosporine, tacrolimus is less likely to induce hypertension, hyperlipidemia, hirsutism and gingival hypertrophy. Familiarity with these toxicities is important as the decision to choose one drug over the other is influenced by the drug's side effect profile - avoiding CsA in adolescents or tacrolimus in Type II diabetes mellitus, for example.

Antiproliferative agents are key adjuncts in transplant immunosuppression based on their ability to curb immune response by inhibiting proliferation of activated T and B cells. **Azathioprine** (Imuran, Prometheus), an inhibitor of

81

nucleotide synthesis, has been used in renal transplantation since 1962. Mycophenolate mofetil (MMF) (CellCept, Roche), a potent inhibitor of the de novo pathway for purine synthesis was introduced in 1995 and quickly gained wide acceptance based on its superiority to azathioprine in preventing acute rejection when combined with either cyclosporine or tacrolimus.[5] As such, the use of azathioprine has significantly declined and the combination of tacrolimus and MMF (with or without corticosteroids) is the preferred combination after kidney transplantation in most centers.

Major side effects of MMF are gastrointestinal and hematologic. Diarrhea can occur in up to one third of patients and maybe associated with nausea, bloating and vomiting. Although MMF specifically targets lymphocytes, leukopenia, anemia and thrombocytopenia may also occur. These side effects generally respond to dose reduction. Recently, an enteric-coated mycophenolic acid has been introduced to reduce gastrointestinal symptoms associated with mycophenolate mofetil. Thus far the new agent has shown equal efficacy with MMF but failed to reduce GI complaints, implying that the toxicity is related to the systemic levels of the active compound mycophenolic acid rather than a local effect.

Sirolimus (Rapamune, Wyeth) is also a macrolide antibiotic, discovered in a soil sample on Easter Island and named for the indigenous population, the Rapanui. The drug, approved by the FDA in 1999 for use in prophylaxis of rejection in renal transplant patients,[6] is structurally similar to tacrolimus, but its action is distinct from that of the calcineurin inhibitors. Sirolimus inhibits signal transduction pathways resulting in inhibition of T-cell proliferation.

The major side effects of rapamycin are myelosuppression and hyperlipidemia. The main advantage of sirolimus over calcineurin inhibitors is its lack of nephrotoxicity. This drug has been used either as primary therapy (calcineurin inhibitor avoidance) or to facilitate withdrawal of calcineurin inhibitor. However, as a primary agent sirolimus showed disappointingly higher rates of rejection and significant problems with wound healing.

Corticosteroids are nonspecific anti-inflammatory agents that partially disrupt activation of T cells and macrophages by inhibiting key cytokines in the inflammatory cascade. These drugs have been a key part of our immunosuppressive regimen since the 1960s and continue to be used in combination with newer agents although at much lower doses. Corticosteroids are associated with a myriad of side effects that increase the risk of serious cardiovascular disease and other morbidities. These include hypertension, dyslipidemia, glucose intolerance, osteoporosis and weight gain to name a few. These serious adverse effects prompted earlier attempts at steroid withdrawal after kidney transplantation. However, investigators noted a substantial increase in acute rejection rates prompting reluctance in adapting such protocols. More recently, under the protection of stronger induction immunosuppression, favorable results have been achieved with rapid steroid withdrawal within the first week after transplantation or with complete steroid avoidance. Corticosteroids, once the mainstay of transplant immunosuppression, are now usually used in small doses (< 0.1 mg/kg/d) or not at all.

TREATMENT OF ESTABLISHED REJECTION

Acute rejection is a major risk factor for reduced short- and long-term graft survival. These episodes reflect inadequate immunosuppression either from aggressive weaning of immunosuppression or patient noncompliance. In most cases, the patient is asymptomatic; the only clue being a precipitous rise in the serum creatinine. Definitive diagnosis rests on a tissue biopsy and treatment involves intensifying immunosuppression by giving high doses of corticosteroids, increasing the doses of maintenance therapy and converting to more potent agents such as tacrolimus and MMF. In more aggressive cases, use of anti-T cell antibodies may be indicated. Recent data show a significant drop in both early and late acute rejection rates, a trend largely attributed to the introduction of new and more potent immunosuppressive agents.

TRENDS

For many years, the transplant community relied on very potent immunosuppression to prevent rejection with the notion that the benefits from heavy immunosuppression far outweigh the risks. However, despite impressive reduction in acute rejection rates, there have been only modest improvements in long term graft outcomes. The main causes of late allograft failure are chronic allograft damage (chronic nephropathy, coronary vasculopathy, recurrent HCV, e.g.) and death from cardiovascular disease, which is exacerbated by chronic immunosuppression. Immunosuppressive medications promote infection, glucose intolerance, dyslipidemia and nephrotoxicity. Hence, there is at present a shift in focus towards striking a balance between adequate immunosuppression on one hand and minimization of adverse effects on the other.

The development of newer immunosuppressive agents has substantially increased treatment options. In the pipeline are drugs that selectively inhibit only T cells that react to donor antigens thus, achieving a state of donor specific tolerance while maintaining a fully functional immune system. Other agents that are being developed are those that selectively block accessory molecules crucial in the recruitment of inflammatory cells into the allograft; as well as agents that alter T-cell trafficking by driving T-cells into lymphoid tissues and away from the graft.[7] How these newer agents will apply to clinical practice remains to be seen.

Newer strategies are also emerging. The concept of "one size fits all" has been abandoned for a more individualized approach, taking into account the patient's immunologic and comorbid risks. While maintaining low rejection rates remains crucial in the early stages of engraftment, minimizing immunosuppression after 6-12 months is as important in improving long term outcomes. The availability of newer agents has substantially increased treatment options and potential combinations allowing greater flexibility in tailoring immunosuppression based on the patient's clinical profile. To this objective, several strategies such as tolerance induction (permanent acceptance of the graft without need for chronic immunosuppression),

early minimization of steroid exposure or even complete avoidance, minimizing exposure to calcineurin inhibitors, utilization of highly potent induction therapy followed by low dose immunosuppression monotherapy are all being actively pursued. Valuable data from all these trials are accumulating; from this flurry of new information there is optimism for improved long-term patient outcomes. These evolving protocols and options highlight the requirement for lifelong follow-up of allograft recipients by a team of transplant specialists.

REFERENCES

1. Merrill JP, Murray JE, et al. Successful homotransplantation of the kidney between nonidentical twins. *NEJM* 1960;262:1251.
2. Calne RY, White DJ, et al. Cyclosporine A in patients receiving renal allografts from cadaver donors. *Lancet* 1978; 2: 1323-7.
3. Gaber AO, First MR, et al. Results of the double blind, randomized, multicenter, phase III clinical trial of thymoglobulin versus ATGAM in the treatment of acute graft rejection episodes after renal transplantation. *Transplantation* 1998; 66: 29-37.
4. Mayer A, Dmitrewski J, et al. Multicenter randomized trial comparing tacrolimus (FK506) and cyclosporine in the prevention of renal allograft rejection. *Transplantation* 1997; 64: 436-43.
5. The Tricontinental Mycophenolate Mofetil Renal Transplantation Study Group A. A blinded, randomized, clinical trial of mycophenolate mofetil for the prevention of acute rejection in cadaveric renal transplantation. *Transplantation* 1996; 61: 1029-37.
6. Kahan BD. The Rapamune US Study Group. Efficacy of sirolimus compared with azathioprine for reduction of acute renal allograft rejection. *Lancet* 2000; 356: 194-202.
7. Hardinger KL, Koch MJ, Brennan D. Current and future immunosuppressive strategies in renal transplantation. *Pharmacotherapy* 2004; 24:1159-76.

Angelito Yango, MD, is Assistant Professor of Medicine, Brown Medical School.

Amit Johnsingh, MD, is a Renal Fellow, Brown Medical School.

CORRESPONDENCE

Angelito Yango, MD
Rhode Island Hospital APC 921
593 Eddy Street
Providence RI 02903
phone: (401) 444-8345
E-mail: ayango@lifespan.org

Considerations for the Inpatient Care of Solid Organ Recipients

Kevin M. Lowery, MD, and Reginald Y. Gohh, MD

Advances in the management of patients with solid organ transplants and improvements in immunosuppression have resulted in prolonged patient and allograft survival. These advancements have, in turn, led to an increase in the number of patients undergoing solid organ transplantation: in 2005, over 28,000 patients in the United States received a solid organ transplant.[1] Because the majority survive more than 10 years after transplantation, physicians in all fields will care for these patients in their practices. While most interactions will likely involve outpatient evaluations and procedures, these encounters will offer the largest variety of challenges in the inpatient setting. Most transplant centers utilize a team approach to managing post-transplant patients. This "team" often includes, but is not limited to, transplant surgeons, medical sub-specialists in the transplanted organ's field, infectious disease specialists, pharmacists, social workers, and nurses. While close interaction with this transplant team remains of utmost importance in all aspects of allograft recipient's care, it is important that all physicians become familiar with the select facets of medicine

that this growing population presents. This article will summarize these challenges and review the most recent recommendations for the inpatient management of solid organ recipients.

Many physicians have some education related to solid organ transplantation, but few have sufficient experience to adjust immunosuppressive agents. In most instances, maintenance of the patient's oral immunosuppressive medication is preferred; however, several circumstances may arise where this is either not necessary or not an option. Whether a plan of care for a clinical situation or a pre-test precaution, inpatients frequently are required to maintain a **Nothing Per Oral (NPO)** status. When an NPO status is expected to be minimal in duration (less than 12 hours), it is often acceptable to withhold the administration of oral immunosuppressive agents until the status is changed and re-start with the prescribed dosing schedule at that time. For longer durations, however, conversion to an **intravenous (IV)** preparation is recommended. Corticosteroids, cyclosporine, tacrolimus, azathioprine, and mycophenolate mofetil are all avail-

able as IV preparations. Sirolimus is not available in IV form in the United States, and can either be transiently discontinued or supplanted with increased IV dosing of other immunosuppressive medications when oral administration is not feasible. Furthermore, it may be necessary to temporarily discontinue all immunosuppressive medications in circumstances where it is felt a more robust immune response may alter a life-threatening situation. Although no specific guidelines are available for medical management in these situations, there is some evidence that the upsurge of cytokines associated with sepsis and severe illness may protect against allograft rejection.[2] In such instances, clinical monitoring is of chief importance, as immunosuppression should be reintroduced as soon as the clinical recovery begins to avoid allograft rejection.

The dosing and administration of immunosuppressive medications in the inpatient setting can also be potentially problematic with regards to poly-pharmacy. While immunosuppressive regimens will vary, **calcineurin inhibitors (CNI)** remain a mainstay for the major-

Table 1

Immunosuppressant	Medication	Mechanism	Effect
Calcineurin Inhibitors: (cyclosporine, tacrolimus) Sirolimus	diltiazem, verapamil, erythromycin, oral contraceptives, -azoles, amiodarone	Inhibit P450-3A4 enzymes	Increase blood concentrations
	phenytoin, rifampin, cholestyramine, octreotide	Interfere with intestinal absorption	Decrease blood concentrations
	phenytoin, phenobarbital, rifampin, nafcillin	Induce P450-3A4 enzymes	Decrease blood concentrations
	ACE inhibitors, NSAIDs, acyclovir, gancyclovir, amphotericin B, -glycosides	Similar toxicity profile	Potential for increased nephrotoxicity when used in combination with CNI
	Statins (pravastatin excluded)	Metabolism decreased by CNI	Increased risk of rhabdomyolysis
Azathioprine	allopurinol	Inhibits metabolism of azathioprine	Increase blood concentrations
	warfarin	Unclear interaction	Decreased effect of warfarin
Mycophenolate Mofetil	cholestyramine, metronidazole	Decreased enterohepatic circulation	Decrease blood concentrations
	probenecid	Inhibits renal tubular secretion	Increase blood concentrations

ity of solid organ transplant recipients. The two CNIs in use today (cyclosporine and tacrolimus) and the antimetabolite drug sirolimus are primarily metabolized and eliminated by the cytochrome P450-IIIA4 enzyme system. Therefore, patients utilizing these medications are at high-risk for numerous drug interactions. Use of medications that induce or inhibit the cytochrome P450 system are not contraindicated for these patients, but close monitoring of organ function as well as cyclosporine, tacrolimus, or sirolimus levels should be maintained when introducing or discontinuing such medications. Additionally, many medications may inhibit or enhance absorption of immunosuppressive medications and alter the levels of these medications. (Table 1)

Cardiovascular disease (CVD) remains a major cause of morbidity in organ transplant recipients and remains the leading cause of death among kidney allograft recipients.[3] The elevated risk of CVD in this population is due to a variety of factors related to both pre-existing (pre-transplant) risk factors as well as variables specific to the post-transplant setting. In renal allograft recipients, the pre-transplantation prevalence of hypertension, diabetes mellitus, hypercholesterolemia, and obesity are 80%, 55%, 60%, and 30% respectively.[4] Additionally, a number of these CVD risk factors are associated with or exacerbated by immunosuppressive drugs. Calcineurin inhibitors and corticosteroids are associated with an increased risk of hypertension, diabetes mellitus, and lipid abnormalities and sirolimus commonly causes hyperlipidemia .[5, 6] While mortality secondary to CVD in non-renal solid organ allograft recipients is lower than renal allograft recipients, the complications seen with these immunosuppressive agents is universal, and the prevalence of CVD will likely rise in these populations as well with longer allograft survivals being seen today.

Corticosteroids and CNI predispose patients to developing post-transplantation diabetes mellitus (PTDM). Corticosteroids impair insulin production, impede the activation of the glucose/FFA cycle, impair glucose uptake in the musculature, and decrease the number and affinity of insulin receptors.[7] The calcineurin inhibitors, cyclosporine and tacrolimus, are postulated to diminish beta

cell insulin production through inhibition of specific cellular proteins.[8] While PTDM can be treated similarly to Type II diabetes mellitus, special considerations regarding contraindications or potential side effects of the available oral agents must be made. Impaired liver or renal function may pose increased risks of hypoglycemia with sulfonylurea agents, and are contraindications, along with congestive heart failure, for use of metformin. Given the limitations of oral agents, and the necessary exposure to immunosuppressive medications, a majority of patients with PTDM eventually require exogenous insulin treatment.[8] During episodes where immunosuppressive doses (in particular corticosteroids) are altered, large variations in blood glucose levels can be expected and diligence in monitoring is of paramount importance.

...most physicians will likely at some point be involved in the routine care of such patients.

Because most transplant recipients are maintained on corticosteroids, adrenal insufficiency is a theoretical concern in the inpatient setting, but rarely a practical one. Since the current standard of care for routine maintenance immunosuppression generally involves relatively low corticosteroid doses (5-10mg of prednisone daily) patients usually have sufficient reserve to respond to stress. Several prospective studies demonstrated that augmentation of baseline steroid doses in various settings of stress (sepsis, surgery, metabolic abnormalities) is unnecessary and may not entirely be benign.[9-11] However, if the patient has signs or symptoms of adrenal insufficiency, the use of high-dose steroids (50-100 mg of hydrocortisone every 8 hours) should be initiated with a return to baseline dosage over a period of 2-3 days as clinical status permits.

Although, when available, renal transplantation remains the treatment of choice for end-stage renal disease, transplantation usually falls short of replacing renal function to normal levels. The average glomerular filtration rate of kid-

ney transplant recipients rarely exceeds 50 mL/min/2.73m² as estimated by an equation derived from the Modification of Diet in Renal Disease (MDRD) study.[12] Recipients of other solid organ transplants are at risk for diminished renal function as well; most likely a result of the nephrotoxicity related to long-term exposure to immunosuppressive agents, in particular calcineurin inhibitors. Approximately 32% of heart recipients, 20% of lung recipients, and 18% of liver recipients have chronic kidney disease (CKD) at 5 years post-transplantation; and up to 29% of these individuals will eventually require some form of renal replacement therapy.[13] In an inpatient setting, this underlying CKD may predispose patients to fluid and electrolyte abnormalities and to toxic accumulation of anesthetic or analgesic medications. It is important to also keep in mind that renal allografts lose their innate ability to autoregulate renal blood flow due to functional denervation of a transplanted kidney, thus predisposing these patients to episodes of ischemic acute renal failure.

Infection remains one of the most common complications of immunosuppressive therapy. Since the vulnerability to infection is related to both pathogenic exposure and the overall immunosuppressive state, the risk for developing specific types of infections is dependent on the time period post-transplant. Immediately post-transplant, patients will be most at risk for pathogens commonly seen in non-immunosuppressed surgical patients. From 1-6 months post-transplant, while immunosuppression dosing remains relatively high, viral and opportunistic infections become more prevalent. The majority of patients receive prophylaxis against cytomegalovirus (valganciclovir), pneumocystis carinii and nocardia (TMP-SMZ) and fungal infection during this period. Beyond six months, for patients with stable allograft function and lower immunosuppressive regimens, infections seen in the general population are again most common, although viral pathogens can appear at any time and the clinical course for viral and bacterial infections is often prolonged.[14] As a result, these patients often require a longer duration of antibiotics and antiviral medications.

87

Immunosuppression also predisposes all transplant recipients to delayed wound healing as a result of diminished tensile strength and tissue integrity. Even at low doses, corticosteroids impair tissue integrity and are associated with capillary and tissue friability.[15, 16] For this reason, it is recommended that skin staples be kept in place 2-3 times longer in the transplant recipient and many transplant surgeons recommend the use of nonabsorbable sutures whenever possible. Recent information has implicated the use of sirolimus with delayed wound healing in the immediate post-transplantation setting when compared to the use of tacrolimus.[17] No data are available thus far as to whether or not this increased propensity toward delayed wound healing with sirolimus carries over to subsequent surgeries, but this should be considered in these situations.

In conclusion, the number of solid organ transplant recipients in the United States is steadily increasing. As a result, most physicians will likely at some point be involved in the routine care of such patients. While close involvement of a team of transplant specialists during these interactions remains the standard for care of all such patients, it is important that all physicians obtain a general understanding of the unique aspects of care presented by this population.

REFERENCES

1. Organ Procurement and Transplantation Network. www.optn.org. Accessed October 26, 2006.
2. Burke GW, Ciancio G, et al. Association of interleukin-10 with rejection-sparing effect in septic kidney transplant recipients. *Transplantation* 1996; 61: 1114-6.
3. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 1998; 32: S112-9.
4. Ojo AO. Cardiovascular complications after renal transplantation and their prevention. *Transplantation* 2006; 82: 603-11.
5. Kasiske BL. Epidemiology of cardiovascular disease after renal transplantation. *Transplantation* 2001; 72: S5-8.
6. Brattstrom C, Wilczek HE, et al. Hypertriglyceridemia in renal transplant recipients treated with sirolimus. *Transplantation Proceedings* 1998; 30: 3950-1.
7. Bialas MC, Routledge PA. Adverse effects of corticosteroids. *Adverse Drug Reactions Toxicological Reviews* 1998; 17: 227-35.
8. Montori VM, Velosa JA, et al. Posttransplantation diabetes. *Diabetes Care* 2002; 25: 583-92.
9. Bromberg JS, Alfrey EJ, et al. Adrenal suppression and steroid supplementation in renal transplant patients. *Transplantation* 1991; 51: 385-90.
10. Glowniak JV, Loriaux DL. A double-blind study of perioperative steroid requirements in secondary adrenal insufficiency. *Surgery* 1997; 121: 123-9.
11. Kehlet H, Binder C. Adrenocortical function and clinical course during and after surgery in unsupplemented glucocorticoid-treated patients. *Brit Med J* 1973; 2: 147-9.
12. Poge U, Gerhardt T, et al. MDRD equations for estimation of GFR in renal transplant recipients. *Am J Transplantation* 2005; 5: 1306-11.
13. Ojo AO, Held PJ, et al. Chronic renal failure after transplantation of a nonrenal organ. *NEJM* 2003; 349: 931-40.
14. Fishman JA, Rubin RH. Infection in organ-transplant recipients. *NEJM* 1998; 338: 1741-51.
15. Anstead GM. Steroids, retinoids and wound healing. *Adv Wound Care* 1998; 11: 277-85.
16. Meadows EC, Prudden JF. A study of the influence of adrenal steroids on the strength of healing wounds. *Surgery* 1953; 33: 841-8.
17. Dean PG, Lung WJ, et al. Wound-healing complications after kidney transplantation. *Transplantation* 2004; 77: 1555-61.

Kevin M. Lowery, MD, is a Renal Fellow, Brown Medical School.

Reginald Y. Gohh, MD, is Associate Professor of Medicine, Brown Medical School.

CORRESPONDENCE
Reginald Gohh, MD
Rhode Island Hospital APC 921
593 Eddy Street
Providence RI 02903
phone: 401-444-8345
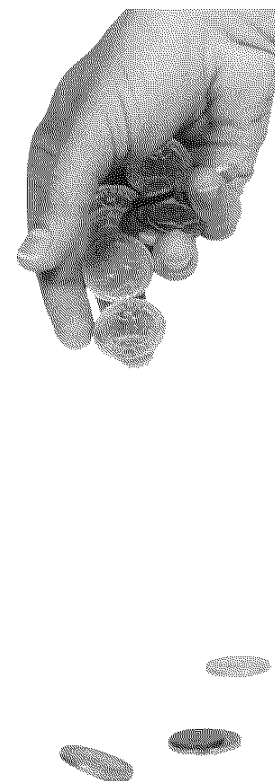E-mail: rgohh@lifespan.org

Is There a Rational Solution to the Kidney Shortage?

Anthony P. Monaco, MD

The treatment of mortal and morbid diseases with organ replacement is one of the great medical miracles of the 20th century. This is particularly true in the case of kidney transplantation, the commonest solid organ transplant, where transplantation produces not only a better quality of life, but also prolongs longevity compared to dialysis.[1] This happy circumstance has dramatically increased the number of patients eligible for kidney transplantation but at the same time has underscored the severe shortage of kidneys for transplantation. Less than 15% of some 70,000 Americans on the kidney waiting list in 2005 received transplants; by 2010 the waiting list will exceed 100,000.[2] As a direct consequence of the kidney shortage, waiting times on dialysis, already 5-10 years in some regions of the country, continue to increase, leading to increased dialysis-associated cardiovascular morbidities and mortality in those patients who are eventually transplanted.[3] Sadly annual death rates on the dialysis waiting list have increased by almost 25% over the past four years.[4]

In the face of this kidney shortage there have been only modest increases in the number of **deceased donor (DD)** kidneys in recent years, essentially achieved by using so-called marginal donors, i.e., extended criteria donors (older, hypertensive donors frequently dying of cerebrovascular causes) and donors after cardiac death (donors who expire without controlled cardiorespiratory support), both circumstances contributing to kidneys of lesser quality. Recently, the US Department of Health and Human Services initiated the Organ Donation Breakthrough Collaborative, a national drive to increase the number of deceased donors. This effort will have the additional benefit of increasing the availability of non-renal solid organ transplants as well as kidneys. It is estimated that only approximately 50% of eligible deceased donors eventually come to organ donation.[5] There has been a more substantial increase in the use of living kidney donors: in the past year living donor kidney

transplants exceeded those for deceased donors. The dramatic improvement in effective immunosuppression has eliminated the need for reduced histocompatibility (consanguinous living related donor-recipient pairs); in landmark studies by Terasaki et al[6] kidney transplants from friends, spouses, lovers, and other unrelated donors survived as well as living related donor kidneys. The risks of donor nephrectomy (perioperative morality of 0.03% and morbidity of <2%) are well established and generally well accepted.[2] The number of living kidney donors transplanted now approaches 40-50% in many programs. Every effort is employed to utilize appropriate willing donors. A number of thoughtful, well-intentioned strategies have been implemented.[7] Thus, totally altruistic donors—unique individuals who volunteer to donate a kidney to any deserving person—are now considered acceptable (after appropriate psychological evaluation). Similarly, exchanges (swaps) between one or more ABO-incompatible living-donor recipient-donor pairs or crossmatch incompatible pairs (or even combinations thereof) have been pursued. Dr. Paul Morrissey of our Rhode Island Transplant Group has been a national leader in these two concepts. These maneuvers add a few additional transplants to all programs, but their overall effect in extending the donor pool, in my experience, is limited.

Advances in basic science research that would facilitate generation and growth of human solid organs (kidneys) *in vitro* and/or permit transplantation of xenogeneic organs are no doubt years away. The extraordinary effectiveness of kidney transplantation, especially living kidney transplants, to cure kidney disease for a very long time has brought into prime focus the need to consider possible alternatives in the form of rewards and/or financial compensation to expand the donor pool.[2,8,9] Financial compensation (as opposed to reimbursement for expenses incurred or loss of income) for organ donation has been strictly prohibited in the United States by the National Organ Transplant Act (NOTA) which

prohibits any person to acquire any human organ for valuable consideration (money) for use in human transplantation or face fines and imprisonment. This legislation was well intentioned, and basically was designed to protect the poor and disenfranchised from potentially dangerous and unhealthy exploitation by unscrupulous middlemen and avaricious brokers. Such legislation has been quite effective in the United States, but an extensive black market to obtain living donor kidneys—many of marginal quality, transplanted under less than optimal conditions, frequently by surgeons of limited quality and experience—has flourished in a number of countries around the world.[10] The number of American patients that utilize these organ black markets has grown; the presence of such patients seeking post-transplant care is now commonplace in most American programs.

Government prohibition of the unregulated sale of kidneys and other organs to protect the poor from exploitation is appropriate and certainly justified. On the other hand, the idea that any type of gain, reward, or compensation—financial or otherwise—for organ donation is unethical and inherently undesirable does not necessarily follow. Rewards for doing good, for making self-sacrifices, for taking personal risks to help others in one's family, community, or country are evident in every fabric of modern Western society. Numerous examples can be given but perhaps the most obvious example in the United States is voluntary military service. The overwhelming majority of volunteers for the United States military are motivated by idealism and patriotism, but they are also encouraged to volunteer with inducements of paid college educations, enlistment bonuses, reenlistment bonuses, and substantial financial recovery for injury or mortality.[11] It is not surprising that minority group members with limited financial resources are numerically disproportionately represented in the military. Likewise, significant numbers of non-citizen immigrants volunteer for military service, eventually

being rewarded for their service by American citizenship (a route taken by my own father in World War I). Thus, the concept of encouraging and rewarding acts of self-sacrifice and personal risk taking to help others—acts essentially motivated by love, altruism, idealism, patriotism or the like—with valuable considerations (money, etc.) is unequivocally established and considered ethically acceptable, even with the realization that more poorer people will undertake self-sacrifice and personal risk in part to gain the financial rewards.

It is accepted that donor evaluation and workup, operative and postoperative care should be covered by the recipient's medical insurance. Also considered acceptable is reimbursement of donors for travel costs and lost wages. A recent proposal has suggested that donor benefits also include short-term (one year) term life insurance (to cover possible operative mortality) and additional lifetime (Medicare) medical insurance.[2] The inclusion of a direct financial payment subsidy has been considered exploitive and problematical.[12] I think the biggest problem in initiating a system of financial rewards for kidney/organ donation is the fact that both opponents [12,13] and proponents [2,8] of the concept refer to this activity exclusively as buying and selling organs. Buying and selling implies financial negotiation between recipient (buyer) and donor (seller), suggests higher or lower prices in the face of variations in value and quality, and may involve middlemen or brokers. Certainly this is not desirable. We need a government regulated, scrupulously supervised program in which a person or his/her estate receives a fixed valuable enhancement or reward for organ donation. Transplant pioneer, Paul Terasaki, MD of UCLA, suggested that donors be rewarded with a valuable gold medal; the implication being that it could be kept or sold if so desired.[14] I envision a scheme in which a government insurance trust fund is established and administered by a federal agency or commission. A direct financial incentive would be paid to both living donors and heirs of deceased donors as a reward or honorarium for organ donation. The reward would be dispersed by the federal agency after confirmation of organ donation, similar to the payment of an insurance policy. Importantly, in this era of expanding medical expenditures, the reduced financial burden of dialysis costs derived from increased kidney transplantation would make the program revenue neutral.

REFERENCES

1. Wolfe RA, Ashby VB, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of first cadaveric transplant. *NEJM* 1999; 341: 1725-30.
2. Gaston RS, Danovitch GM, et al. Limiting financial disincentives in live organ donation. *Am J Transplant* 2006; 6: 2458-555.
3. Meier-Kriesche HV, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes. *Transplantation* 2002; 74: 1377-81.
4. Merion RM, Ashby VB, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA* 2005; 294: 2726-33.
5. Sheehy E, Conrad SL, et al. Estimating the number of potential organ donors in the United States. *NEJM* 2003; 349: 667-74.
6. Terasaki PI, Cecka JM, et al. High survival rates of kidney transplants from spousal and living unrelated donors. *NEJM* 1995; 333: 333-6.
7. Wessel D. Easing the kidney shortage. *Wall Str J* 17 June 2004.
8. Friedman E, Friedman A. Payment for donor kidneys. *Kidney Int* 2006; 69: 960-2.
9. Monaco AP. Rewards for organ donation. *Kidney Int* 2006; 69: 955-7.
10. Tilney NL. *Transplant: From Myth to Reality*. Yale University Press, New Haven and London 2003:364-74.
11. Brooke J. On the farthest US shores, Iraq is a way to a dream. *NY Times* 31 July 2005.
12. Fox MD. The price is wrong:. *Am J Transplant* 2006; 6: 2529-30.
13. Delmonico F. Commentary: The WHO resolution on human organ and tissue transplantation. *Transplantation* 2005; 79: 639-40.
14. Terasaki PA. Congressional gold medal for transplant donors and families. *Am J Transplant* 2005; 5: 1167.

Anthony P. Monaco, MD, is Professor of Surgery, Harvard Medical School, and Director of Transplant Services, Rhode Island Hospital.

CORRESPONDENCE
Anthony Monaco, MD
Rhode Island Hospital APC 921
593 Eddy Street
Providence, RI 02903
Phone: (617) 632-9822
e-mail: amonoaco@caregroup.harvard.edu
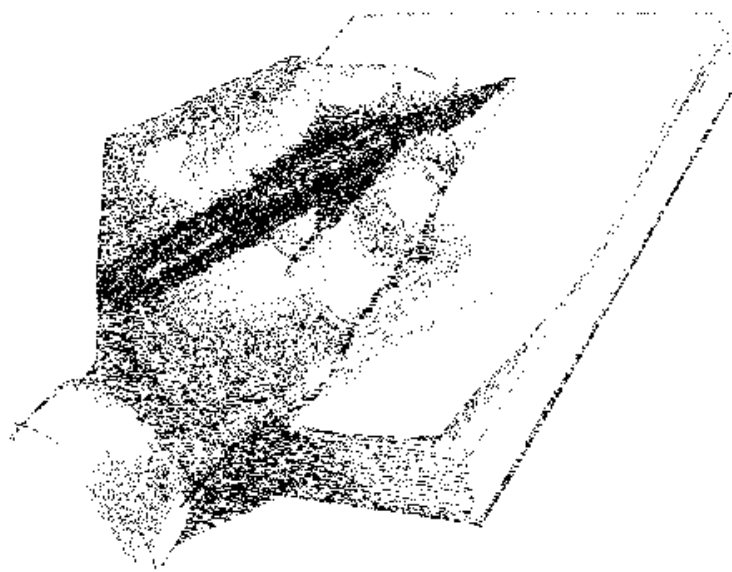
The National Organ Transplantation Breakthrough Collaborative – A Rhode Island Hospital Perspective

Kevin M. Dushay, MD, FCCP, and Suzanne Duni Walker, Esq, RN, BSN

As of November 27, 2006, close to 94,000 people in the United States were waiting for organ transplants, compared to fewer than 75,000 in 2000. The number of patients dying while waiting for transplants rose from 6,500 in 2000 to 7,300 in 2004. In New England (Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, and Connecticut) nearly 4,000 individuals are wait-listed for organ transplants; in Rhode Island the figure is over 250. In 2004, only 51% of potential organ donors provided organs for transplantation.[1]

This disparity spearheaded the **first Organ Donation Breakthrough Collaborative (ODBC)** in October 2003. Representatives of the US Department of Health and Human Services along with organ transplantation and hospital professionals began a year-long program to achieve greater access to donor organs for transplantation. A second Organ Donation Breakthrough Collaborative followed, and over the past year, the **first Organ Transplantation Breakthrough Collaborative (OTBC)** was convened. Collaborative members have used techniques developed at the Institute for Healthcare Improvement under the direction of Donald M. Berwick, MD, to disseminate best practices for increasing both the number of organ donors and the number of organs procured per donor. Principally these changes involved increasing consent rates and relaxing arbitrary exclusion criteria when data indicate acceptable recipient and graft survival rates.

Rhode Island Hospital/Hasbro Children's Hospital, the only organ transplant center in Rhode Island, has been a member of all three breakthrough collaborative sessions, represented by teams consisting of **Rhode Island Hospital (RIH)** and **New England Organ Bank (NEOB)** staff. The NEOB is the **organ procurement organization (OPO)** that serves Rhode Island and most of New England. This article is a report to the Rhode Island medical community of the organ donation and transplantation practices that have been implemented over the past year at RIH. We also describe opportunities for physicians to increase the supply of donor organs.

HIGH LEVERAGE CHANGES

The ODBC, and later the OTBC, stressed these goals: [1,2]

1. **Advocate Organ Donation as the Mission**
   Those involved with the entire process, from identifying potential organ donors, to informing families about the opportunity to provide a potentially life-saving organ donation, to caring for the donor, must be enthusiastic about, committed to, and skilled in the practices of organ donation.

2. **Involve Senior Leadership to get Results**
   At RIH, the Senior Vice President of Medical Affairs, Boyd P. King, MD, attends the Organ Donation

Advisory Committee meetings, and meets with its members to provide administrative backing and support

3. **Deploy a Self-Organizing OPO/Hospital Team**
   A **Hospital Relations Coordinator (HRC)**, Suzanne Walker, Esq, RN, BSN, and two **Family Service Coordinators (FSC)**, Leo Trevino and Darlene Fiotto, all employed by the New England Organ Bank, work from an NEOB satellite office within the RIH complex to respond quickly to referrals of potential donors. In addition, they are valuable resources for information and education regarding organ donation. The HRC regularly analyzes hospital-specific data through death record reviews and "After Action Reviews" to identify missed opportunities for organ donation. The FSCs are trained requestors, as well as liaisons to the community, meeting with religious and secular leaders and providing or coordinating community-directed educational programs. Completing the OPO team are the NEOB **Donation Coordinators (DCs)**, who provide on-site continuous management of the organ donor and the donation process. The DC collaborates with the health care team in the critical care of the organ donor, including testing, requesting consults, and directing therapy. At the same time, in conjunction with Newton-based **Organ**

Table 1: Organ Donation Data for Rhode Island Hospital[9]

Year	Organ Donor Referrals	Organ Donors	Organs from RIH Transplanted Anywhere	Organs Transplanted per Donor	NEOB Organs Transplanted at RIH	Total Organs Transplanted at RIH
2003	94	18	51	2.83	39	47
2004	85	18	70	3.89	31	41
2005	75	15	58	3.87	32	43
2006	99	19	64	3.37	30	37

Note: 2006 data are 1/1/06 – 11/27/06

Clinical Coordinators (OCC), they are responsible for allocation and placement of all recovered organs. The DCs coordinate the surgical teams, technicians, operating room staff, and transplant centers.

RIH has developed and is expanding a cadre of critical care nurse organ donation champions, who provide education and support to their colleagues. Furthermore, there are RIH respiratory therapists and an Intensivist Physician Champion who have designated themselves as available for assistance in the management of organ donors. RIH social workers join the OPO/Hospital organ donation team to provide family support.

4. **Practice Early Referral, Rapid Response**
Families are rarely prepared for end of life decisions when a loved one is a victim of trauma or a sudden neurologic event. Information often must be presented several times. Success in obtaining consent for organ donation is enhanced when families do not feel rushed by health-care professionals, when expert, sensitive, and confident individuals answer questions, and when information is available at the time it is requested.[3]

5. **Master Effective Requesting**
Studies have shown that the highest consent rates are achieved when physicians refer families to OPO personnel for discussion regarding the opportunity to donate a loved one's organs. In addition, physicians should support the offer of organ donation as an opportunity to save a life, rather than as a legal requirement at the time of a patient's anticipated death.[3] Physicians must recognize the possibility of an appearance of a conflict of interest in the family's mind when they tell a family that their loved one's prognosis is poor and then speak of organ donation. First and foremost, families want to hear from their doctor that he or she is doing everything possible for their loved one. After an interval, the doctor must ensure that the family understands that their loved one is not going to survive, *before* they are approached regarding organ or tissue donation, regardless of who is doing the requesting.

The patient should be fully supported until organ donation has been absolutely ruled out if we are to reduce the number of patients dying on the waiting list.

---

6. **Implement Donation after Cardiac Death**
The number of brain-dead potential donors has always been less than the number of patients waiting for transplants. Even with optimal consent rates and optimal numbers of organs procured, some patients will be on waiting lists. Patients not succumbing to brain death should still have the right to donate their organs to others who will otherwise die. In addition, their families are entitled to the solace that comes from the donation of life-saving organs. However, many donor hospitals do not have policies to provide the option of donation after cardiac death to their patients who wish to do so. This is a disservice, not only to patients who wish to bestow this gift, but to other patients who might be recipients of that gift.

ACTIONS TAKEN OVER THE PAST YEAR AT RHODE ISLAND HOSPITAL

Clinical Triggers
A set of criteria indicating a patient is appropriate for referral to the NEOB have been developed, printed on laminated pocket-sized cards, and distributed to staff in the Emergency Room and Critical Care Units. Any patient $\leq$ 85 years old with a Glasgow Coma Scale of = 4 due to neurologic insult, or in whom terminal extubation or no resuscitation status is being considered, is a potential organ donor and should be discussed with the NEOB (phone: 800-446-NEOB). The suitability of a donor organ depends on the prognosis of each potential recipient without it; therefore, the decision to reject a possible donor organ should be made in consultation with transplant centers.

Donation Team Huddles
These brief meetings, involving the NEOB on-site coordinator(s), the patient's nurse and/or physician(s) and/or other healthcare providers, the unit social worker, and any other appropriate individuals, are held as soon as possible after referral of a potential organ donor, and periodically thereafter, in order to determine the best manner and timing for approaching the family to discuss the opportunity for donation.

After Action Reviews
These meetings review the course of recent referrals to the NEOB. Previously, these meetings were held quarterly, but will now be held weekly or biweekly so staff will have a clear memory of cases. This will minimize the risk of losing subsequent donors to repeated suboptimal practices.

Real Time Death Record Reviews
These reviews identify potential donors who were not referred to the NEOB at all. The patients' healthcare providers are informed of these missed opportunities.

Identify Physician/Clinician Champions
For the most part, physicians committed to increasing the number of donor organs are not born, they are made. Until recently, most OPOs had their DCs relieve physicians of the responsibility of caring for their patients once they had died and made the transition from patient to organ donor. As a result, most physicians have little to no experience caring for patients following brain death. A profound series of pathophysiologic derangements occur in the brain dead patient.[4,5] Superimposed on the pathophysiology of brain death are the iatrogenic complications often present following unsuccessful resuscitation of the severely brain injured patient. The Organ

Transplantation Breakthrough Collaborative has promoted the need to involve intensivists in the management of organ donors, based on data demonstrating more organs transplanted per donor when intensivists care for donors, and when donor management guidelines are followed and achieved.[6-8]

Even prior to obtaining consent for organ donation, physicians can potentially help increase the number of organs procured per donor. Often physicians become less aggressive in patient management after telling a family the patient's poor prognosis and discussing the option of withdrawing cardiopulmonary support. Physicians do not want to prolong the dying process for the patient or the suffering of the family. However, the process of obtaining consent for organ donation may require multiple discussions extending over hours, even days. During this time, potential organ donors may fall into a "therapeutic hole" with worsening hemodynamics, metabolic derangements, and failing organs. Once consent for organ donation is obtained, the NEOB Donation Coordinator and/or physician may resume aggressive care only to find irreversible organ damage precluding donation. The patient should be fully supported until organ donation has been absolutely ruled out if we are to reduce the number of patients dying on the waiting list.

RESULTS

Over the years 2003, 2004, and 2005, the number of organ donors and organ transplants in New England remained relatively stable, but at levels higher than those in 2000 and earlier. (Table I) At the 2nd Annual National Learning Congress on Organ Donation and Transplantation in October 2006, the NEOB was recognized for its sustained high rate of **Donation after Cardiac Death (DCD)** donors over the past year, given a Donation Service Area performance award for outstanding performance in multiple aspects of organ donation, and a National Improvement Leader Award. The staff of the NEOB developed and implemented the second largest DCD program among 58 OPOs in the United States. At the same event, RIH won an Organ Donation Medal of Honor for its high rate of obtaining consent for organ donations.

SUMMARY

Patients needing organ transplants still exceed the number of organs, and each year some patients on waiting lists die. A series of national collaborative meetings identified practices shown to increase organ donation consent rates and organs procured per donor. A partnership between the NEOB and donor hospitals is important to achieve these goals. By following best practices set forth by the Collaborative movement and put in place by NEOB, physicians can increase the supply of donor organs in New England and nationally.

REFERENCES

1. Organ Transplantation Breakthrough Collaborate Charter, 2nd Annual National Learning Congress on Organ Donation & Transplantation. New Orleans, LA, October 2006.
2. Organ Donation Breakthrough Collaborative, First Annual National Learning Congress. Pittsburgh, PA, May 2005.
3. Siminoff LA, Gordon N, et al. Factors influencing families' consent for donation of solid organs for transplantation. *JAMA* 2001; 286:71.
4. Szabó G. Physiologic changes after brain death. *J Heart Lung Transplant* 2004; 23: S223.
5. Wood KE, Becker BN, et al. Care of the potential organ donor. *NEJM* 2004; 351:2730.
6. Personal communication, Christopher C. Curran, Organ Operations, New England Organ Bank, Newton, Massachusetts.
7. Rosendale JD, Chabalewski FL, et al. Increased transplanted organs from the use of a standardized donor management protocol. *Am J Transplant* 2002; 2:761.
8. Rosendale JD, Kauffman M, et al. Aggressive pharmacologic donor management results in more transplanted organs. *Transplantation* 2003; 75:482.
9. Personal communication, Jim Bradley, Clinical Information Systems, New England Organ Bank, Newton, Massachusetts.

Kevin M. Dushay, MD, FCCP, is Assistant Professor of Medicine, Brown Medical School.

Suzanne Duni Walker, Esq, RN, BSN, is Hospital Relations Coordinator, New England Organ Bank.

CORRESPONDENCE:

Kevin M. Dushay, MD, FCCP
Pulmonary, Critical Care & Sleep
Disorder Medicine
Rhode Island Hospital
593 Eddy Street – APC 7
Providence, RI 02903
phone: 401-444-3565
E-mail: Kevin_Dushay@brown.edu

Brown Med
BROWN MEDICAL SCHOOL
Division of Geriatrics
Department of Medicine

GERIATRICS FOR THE PRACTICING PHYSICIAN

QUALITY 2 PARTNERS OF RHODE ISLAND

Quality Partners of RI
EDITED BY ANA C. TUYA, MD

The Assessment and Management of Falls Among Older Adults Living In the Community

Michael P. Gerardo, DO

A 78-year-old man presents to your office for the first time. A review of his medical record reveals a problem list that includes hypertension, atrial fibrillation, osteoarthritis, depression and a previous transient ischemic attack. His medication list includes metoprolol, warfarin, acetaminophen, omeprazole, escitalopram oxalate, and aspirin. He tells you that although he has been educated on the proper use of his cane, and encouraged to use it, he does so intermittently; "when I feel off-balance." He adds that his vision is not as good as it used to be. On more direct questioning, he reports that he has been afraid of falling since last winter. He stumbled on a patch off ice and since then has noticed that he is not as quick or steady on his feet as he would like.

This case illustrates the typical presentation of older adults at risk of falling. The exact cause of falling is often difficult to pinpoint because numerous contributing factors (such as age-related changes, diseases commonly occurring with aging, multiple co-morbidities and the medications used to treat them) can be identified in an older adult. The goal of this edition of the column is to provide an evidenced-based approach to fall prevention. I begin with a discussion of the scope of the problem facing clinicians, and proceed to a model for assessment and intervention; at the conclusion of this article are the well-established clinical guidelines for fall prevention among older adults living in the community.

IMPACT & ETIOLOGY

Falls represent an enormous psychological, social and financial cost to the individual, family and society. It is estimated that more than one third of community-dwelling persons age 65 or older experience a fall each year, that number increases to 50% among persons over the age of 80.[1,2] The sequelae from a fall are of important consequence. One in ten falls results in a serious injury (e.g. fracture, subdural hematoma, soft tissue or head injury).[3] Falling is the leading cause of injury, and the 6th leading cause of death among individuals over the age of 65.[4] Individuals may acquire disability from injury, fear of falling, or restriction in ambulation, either self-imposed or imposed by family members to prevent subsequent falls. In addition to restriction in mobility, falls place a previously independent person at risk of nursing home placement.[5,6] Falls account for 6% of urgent hospitalizations, and only 50% of those admitted to the hospital after falling are alive one year later.[2]

The majority of falls result from predisposing risk factors or acute perturbations to the limited physiologic reserve of an older person.[7] Impairments in balance, gait, vision and muscle strength increase the risk of falling. In addition, depression, impaired cognition, postural hypotension, the use of four or more medications, and arthritis independently increase the risk of falling.[3] Certain classes of drugs have a clear association with the risk of falling: serotonin reuptake inhibitors, tricyclic antidepressants, neuroleptic agents, benzodiazepines, anticonvulsants, class IA antiarrhythmic medications, and digoxin.[8] Older persons can be particularly susceptible to falls during episodes of acute illness or de-compensated chronic illness, and in the first month following hospital discharge.[9] Environmental hazards, such as rugs, improper footwear, poor lighting, and stairs have been associated with an increased risk of falling.[3,10]

ASSESSMENT & INTERVENTION

The exact age at which to begin screening for the risk of falling is uncertain; however, the prevalence of risk factors for falling increases sharply after age 70.[7] Physicians should at least once a year ask older patients about any falls or the fear of falling. This yearly screen should include questions about and observation for difficulties with balance or gait. The "Get-Up and Go" test is a short screening tool that tests for balance and strength. It involves asking the patient to rise from a chair, walk ten feet, turn, return to the chair and sit. Performing the task longer than 9 seconds confers a two-fold risk of falling. Difficulty with any part of the test may increase risk as well. A timed score that is greater than 30 seconds indicates that the patient is at high risk of falling, and will require assistance due to impaired mobility. Those patients who have not experienced a fall and do not exhibit any balance or gait difficulties should be encouraged by their physician to participate in exercise programs that include balance and strength training.

For those patients who have fallen, are afraid of falling, or exhibit difficulties with gait or balance, identifying relevant risk factors should be the first step in fall prevention. The most successful approach to prevention has been a multifactorial assessment for risk factors, followed by interventions targeting the identified risk factors. It is estimated that this approach can reduce the risk of falling by as much as 39% among older persons living in the community.[11] The clinician should diagnose the underlying cause or refer for an evaluation of a problem with gait or balance. The most successful interventions studied in clinical trials include reducing psychoactive medications; reviewing the medication portfolio for inappropriate or unnecessary medications; using physical or occupational therapy for strengthening, balance and proper use of assistive devices; management of orthostatic hypotension;

94

home safety evaluation for environmental hazards; and referral for evaluation of visual impairments.[12]

GUIDELINES & RECOMMENDATIONS

The US Preventive Services Task Force (UPSTF) recommends that all persons 75 years of age or older be counseled about specific measures to reduce the risk of falling.[13] Persons between the ages of 70 to 74 who have at least one risk factor for falling should also receive the same counseling about risk reduction measures. The American Geriatrics Society, the British Geriatrics Society and the American Academy of Orthopedic Surgeons concertedly recommend that on a yearly basis clinicians should not only ask their older patients about any falls which occurred over the previous year, but also test gait and balance. For those who screen positive by having either experienced a fall or exhibit difficulty with gait or balance, it is recommended that physicians perform a comprehensive assessment, followed by interventions targeting the identified risk factors.[14]

Let us return to the patient described at the introduction of this column. This patient has experienced a fall and should undergo a comprehensive assessment for relevant risk factors. A detailed history reveals the following risk factors for falling: depression, arthritis, use of more than four medications, and improper use of an assistive device. On physical exam, you confirm visual impairment and difficulties with gait and balance, but do not document orthostasis. He does have atrial fibrillation and the rate is well controlled with Metoprolol. His neurologic (proprioception, cognition, and muscle strength) examination was found to be normal. After considering other causes of gait disturbance and based on his musculoskeletal examination, you suspect that his gait impairment, which requires the use of a cane, is due to degenerative joint disease. Based on this comprehensive assessment, a targeted intervention plan would include 1) referral to a physical therapist for gait, balance, and strength training and the proper use of an assistive device, 2) occupational therapy for a home safety evaluation to reduce the number of environmental hazards, and 3) an ophthalmologic exam. The medication portfolio was critically evaluated, but the number of medications was not reduced because the patient required all six medications to effectively manage his chronic illnesses; neither was dosage reduction needed. A year later, after having complied with the recommendations, the patient returns to your office and reports greater confidence in walking with his cane and no falls.

WEB BASED RESOURCES

American Geriatrics Society (http://www.americangeriatrics.org/education/forum)
Centers for Disease Control and Prevention (http://www.cdc.gov)
National Institute on Aging (http://www.nia.nih.gov)

REFERENCES

1. Bergland A., Wyller TB. Risk factors for serious fall-related injury in elderly women living at home. *Injury Prevention* 2004; 10: 308-13.
2. Sattin RW. Falls among older persons. *Annual Rev Public Health* 1992; 13: 489-508.
3. Tinnetti ME, Doucette J, et. al. Risk factors for serious injury during falls by older persons living in the community. *J Ameri Griatrics Soc* 1995; 43: 1214-21.
4. Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS) [database online]. National Center for Injury Prevention and Control, CD). 2001.
5. Tinnetti ME, William CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. *J Gerontol A Biological Medical Sciences* 1998; 53: M112-M9.
6. Tinnetti ME, William CS. Falls, injuries due to falls, and the risk of admission to a nurisng home. *NEJM* 1997;1279-84.
7. Tinetti ME, Speechley M, Ginter SF. Risk factor for falls among elderly persons living in the community. *NEJM* 1988; 319: 1701-7.
8. Leipzig RM, Cummings RG. Tinetti ME. Drugs and falls in older people. *J Amer Geriatric Society* 1999; 47: 30-50.
9. Mahoney J, Sager M, Johnson J. Risk of falls after hospital discharge. *J Ameri Geriatric Society* 1994. 42: 269-74.
10. Tinnetti ME, Preventing falls in elderly persons. *NEJM* 2003; 348:42-9.
11. Gillespie LD, Gillespie WJ, et. al. Interventions for preventing falls in elderly people. *Cochrane Database Systemic Review* 2001; 3: CD000340.
12. Tinnetti ME. Gordon C, et. al. Fall-risk evaluation and management, *Gerontologist* 2006. 46: 717-25.
13. USPSTF, Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. Preventive Service Task Force. 1996, Baltimore: William and Wilkins: 659-85.
14. American Geriatrics Society, American Academy of Orthopaedic Surgeons Panel on Falls Prevention, Guide for the Prevention of Falls in Older Persons. *J Amer Geriatric Society* 2001. 49: 664-72.

Michael P. Gerardo, DO, is a Postdoctoral Research Fellow in Community Health, and a Clinical Fellow in Geriatric Medicine, Rhode Island and Miriam Hospitals.
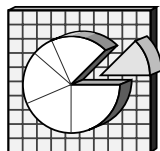
8SOW-RI-GERIATRICS -032007

Classification of Emergency Department Visits:
How Many Are Necessary?

Jay S. Buechner, PhD, and Karen A. Williams, MPH

In a recent year, hospital emergency departments (EDs) in Rhode Island provided care to over 380,000 patients who did not require subsequent admission to an inpatient or observation bed.[1] Many ED visits are for true emergencies that could not be treated in other health care settings, but there has been much discussion among providers, payers, and policy makers on whether some of these patients could have been treated in less intensive and more appropriate settings, had those settings been available, and whether additional ED visits could have been avoided had the patient's primary care been adequate. A recent study has classified ED visits based on whether they are medical emergencies, whether they require care from an emergency department, and whether they are preventable or avoidable with adequate primary care.[2] The results of this study have been applied to emergency department visit data from hospitals in Rhode Island for presentation here.

METHODS

Under licensure regulations, the eleven acute-care general hospitals and two psychiatric facilities in Rhode Island report to the Department of Health a defined set of data items on each emergency department visit beginning with visits occurring January 1, 2005. The data reported includes patient-level demographic and clinical information. This analysis covers ED visits occurring January 1 – December 31, 2005 and is limited to ED visits not resulting in admission to the hospital. Due to complexities in the manner in which hospitals report ED data, the data presented here are subject to change as methods to distinguish ED visits that result in inpatient admission at acute-care facilities from those that do not are improved.

Billings, et al., reviewed approximately 5,700 medical records of ED visits in New York and classified them according to three standards – (1) emergent cases vs. non-emergent cases, (2) cases requiring a level of care provided only by a hospital ED vs. cases treatable in a primary care setting, and (3) cases that were preventable or avoidable with adequate primary care vs. those not preventable or avoidable.[2] (Figure 1) Cases where the first-listed diagnosis was injury, mental health-related, or alcohol or drug-related were not classified. The algorithm resulting from that 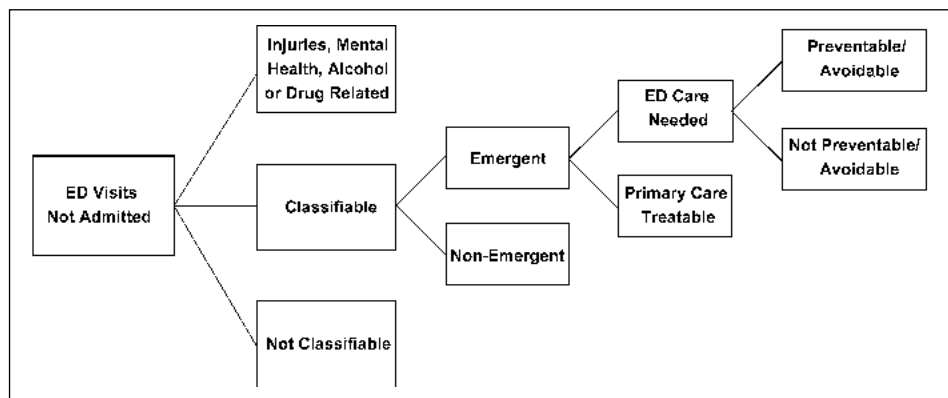study has been applied to the ED visit data submitted from Rhode Island hospitals for calendar year 2005 to produce the estimates presented here. (The Center for Health and Public Service Research at New York University makes available a computer program for use with ED databases,[3] and that program was adapted for use with Rhode Island ED data.)

Figure 1. Classification of emergency department visits

RESULTS

In 2005, there were 382,247 visits to EDs in Rhode Island's acute-care general and psychiatric hospitals that did not result in an inpatient stay. Of these, an estimated 44% were in one of the three categories indicating the ED visit was either unnecessary or avoidable, including 19.8% non-emergent cases, 18.8% emergent cases not requiring the facilities of a hospital ED, and 5.4% emergent cases requiring the facilities of a hospital ED but preventable or avoidable with adequate primary care. (Figure 2) Of the remaining 56% of visits, the majority were for injuries, and a small proportion were related to mental health and substance

Figure 2. Emergency department visits by classification category, Rhode Island, 2005
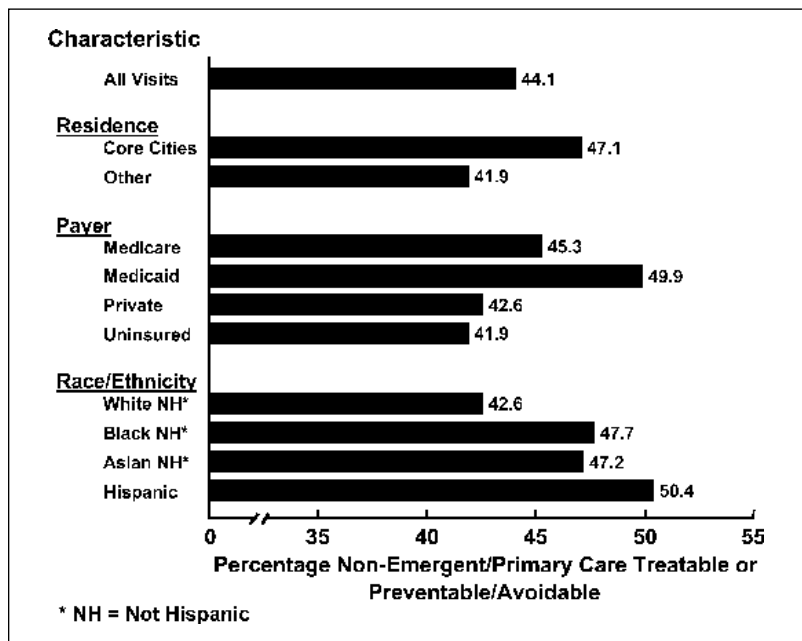
Figure 3. Percent of emergency department visits that are non-emergent, primary-care treatable, or preventable/avoidable, by selected patient characteristics, Rhode Island, 2005

providing a working estimate to inform changes in policy and operation that may result in better care and better outcomes for these patients. Hospital emergency departments have an important role in ambulatory care, but other care settings are better organized to provide continuity of care, patient education, and management of chronic conditions, all of which are hallmarks of a good primary care system.

REFERENCES
1. Williams KA, Buechner JS. Utilization of hospital emergency departments, Rhode Island 2005. *Medicine & Health / Rhode Island* 2006;89:415-6.
2. Billings J, Parikh N, Mijanovich T. Emergency department use in New York City: a substitute for primary care? *Issue Brief.* The Commonwealth Fund. November 2000.
3. http://www.nyu.edu/wagner/chpsr/index.html?p=25. Accessed February 6, 2007.

Jay S. Buechner, PhD, is Chief, Center for Health Data and Analysis, and Assistant Professor of Community Health, Brown Medical School.

Karen A. Williams, MPH, is Public Health Epidemiologist, Center for Health Data and Analysis.

abuse. Approximately 10% fell into categories that could not be classified according to the Billings scheme.

The proportion of ED visits that fell into one of the three categories representing unnecessary or avoidable utilization of the ED varied with patient characteristics. Higher than average proportions were seen among patients who resided in one of the six core cities in Rhode Island (47.1%), who were enrolled in the state's Medicaid Program (49.9%), or who were Hispanic (50.4%), Black (47.7%), or Asian (47.2%). (Figure 3) The lowest proportions were seen among those who were uninsured (41.7%), who lived outside the core cities (41.9%), who had private insurance coverage (42.6%), or who were White (42.6%).

DISCUSSION

The Billings algorithm classified just over half (54.4%) of ED visits at Rhode Island hospitals that did not result in an inpatient admission by whether they were emergent, treatable in a primary care setting, and preventable or avoidable with adequate primary care. Fewer than one-fifth of the classified visits were classified as emergent, not treatable in a primary care setting, and not preventable or avoidable with adequate primary care. The remaining visits can be looked at as an upper-bound estimate of the volume of ED visits in Rhode Island that may be avoidable or treated in other settings under the right circumstances.

There are clearly some caveats needed in applying the Billings methodology to Rhode Island ED data. The classification scheme is based on medical record reviews of 5,700 ED visits during 1994 and 1999 in Bronx Borough, New York City, where access to medical care and patterns of care may be much different than in Rhode Island in 2005. In addition, the data from the 5,700 examined records were used to apportion visits with 659 different principal diagnosis codes, so that most proportions used in the algorithm are based on small numbers of cases and therefore may be imprecise. However, the algorithm is useful in

Bloodborne Pathogen Transmission Potential From Neurological Pinwheels

Robert S. Crausman, MD, MMS, Utpala Bandy, MD, MPH, and Linda Julian

The Occupational Safety and Health Administration (OSHA) defines contaminated sharps as "….any contaminated object that can penetrate the skin including, but not limited to, needles, scalpels, broken glass, broken capillary tubes and exposed ends of dental wires." [29 CFR 1910.1030(a)]

As such the classic neurological pinwheel qualifies as a sharp. Thus, the use of the neurologic pinwheel for neuro-

logic testing must be considered a potential vehicle for person-to-person spread of blood borne pathogens such as HIV, Hepatitis B and Hepatitis C. Moreover, with as many as 20 pins per pinwheel the risk is further increased. Fortunately, disposable and or sterilizable devices exist. Examples include the CleanWheel trademark ®, Cronin pinwheel ™ and others*.

The reusable safety pin should also be considered a potentially contaminated sharp. Although the specific risk for iatrogenic transmission of Hepatitis B, C, and HIV with the use of these neurologic testing instruments has not been clearly defined it is clear that the use of nondisposable or unsterilized reusable pinwheel devices or pins is inconsistent with OSHA regulations which exist to protect both patients and caregivers.

* This reference to named products should not be misconstrued as an endorsement for any specific product by the RI Department of Health.

REFERENCES

Occupational Safety and Health Standards. Toxic and hazardous substances. Bloodborne pathogens. 29 CFR 1910.1030(a)

http://osha.gov/SLTC/bloodbornepathogens/index.html

Durham D, Wasserburger J. Disposable needles should be the only instrument used to test sensation in neurologic examinations. *West J Med* 1997. 166:216-7.

http://www.pubmedcentral.nih.gov/tocrender.fcgi?iid=124762

Robert S. Crausman, MD, MMS, is Chief Administrative Officer, RI Board of Medical Licensure and Discipline, Rhode Island Department of Health, and Associate Professor of Medicine, Brown Medical School.

Utpala Bandy, MD, MPH, is Assistant Medical Director, Center for Epidemiology, Rhode Island Department of Health.

Linda Julian is Complaint Investigator, Health Services Regulation, Rhode Island Department of Health.

CORRESPONDENCE

Robert S. Crausman MD
Chief Administrative Officer
RI Board Medical Licensure and Discipline
3 Capitol Hill
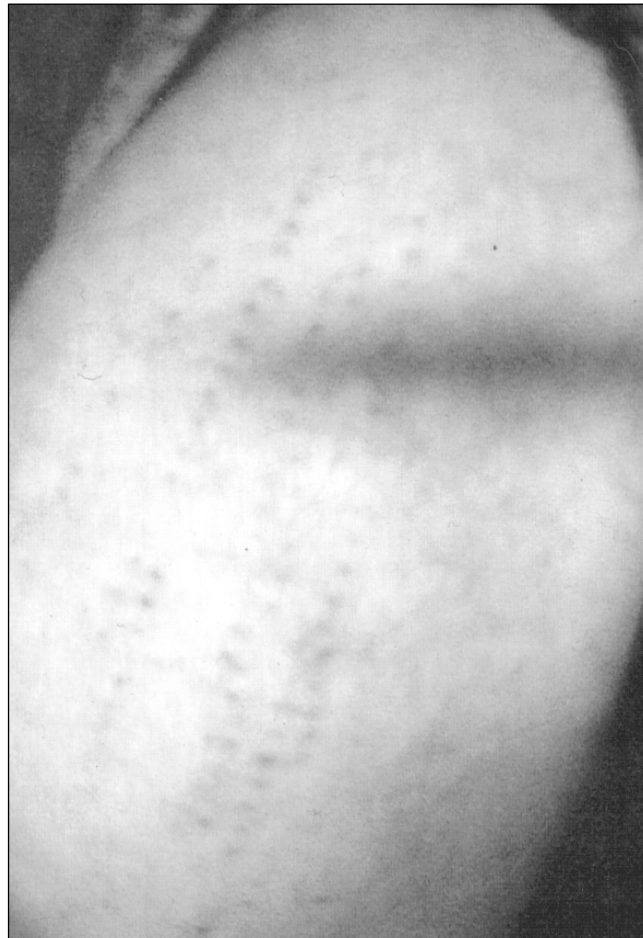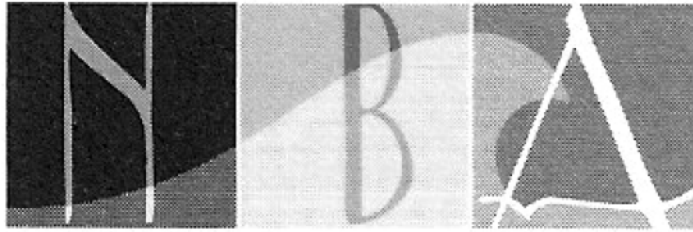Providence RI 02908
e-mail: RSCrausman@aol.com

Figure 1. Lower extremity of a patient demonstrating tissue damage after neurologic examination using a pinwheel device

Figure 2 – Neurologic pinwheel

NARRAGANSETT BAY ANESTHESIA

Anesthesiologist in Chief of the Department of Anesthesiology

Miriam Hospital

The Miriam Hospital is a 247 bed adult medical/surgical Brown Medical School Affiliated Magnet Hospital and a member of Lifespan which is the second largest employer in RI. We are seeking applications and nominations for this position. This opening provides a unique opportunity for an individual to oversee the development of this important clinical department during a time of active growth.

The successful candidate will have superior interpersonal and team building skills that serve to motivate others, demonstrated leadership skills with an understanding of business practices, strategic planning and managing change and outstanding clinical competence with demonstrated expertise in anesthesiology. The successful candidate will also have experience in the training of medical students, residents and other health care professionals. The Chief will oversee 10 new ORs performing complex cardiothoracic and other leading edge minimally invasive procedures including robotics and have a busy 6 room ambulatory center. Pediatrics and obstetrics are not included.

Candidates must have a doctoral degree (M.D./D.O. or equivalent), be board certified by the American Board of Anesthesiology, be eligible for licensure in the state of RI and have proven experience in a leadership position.

The successful candidate will qualify for an appointment at the level of Clinical Associate Professor or Professor at Brown Medical School.

For consideration, please submit a cover letter and current curriculum vitae to:

Plexus Management Group
Email: lromanelli@plexusmg.com
Phone: 781-407-7771
Fax: 781-407-0996

Letters to the Editor

To The Editor,

Dr. Joseph Friedman's stimulating and insightful commentary, "Dreams In Neurological Diseases," [December, 2006] reminded me of the widespread interest in dreams and dreaming in American culture in the 20th Century, expressed by poets and by composers and lyricists who have pondered the fearful, hopeful, painful, wistful, happy, sad and other Freudian complexities of the dream state in many popular songs. A representative but not comprehensive list would include the following :

> I'll See You In My Dreams
> Dream A Little Dream Of Me
> When My Dreamboat Comes Home
> Dream Dancing (one of Cole Porter's best)
> Don't Believe Everything You Dream (music by the talented Jimmy McHugh and cautionary lyric by Harold Adamson)
> All I Do Is Dream Of You (the whole night through)
> Lights Out (Close Your Eyes And Dream Of Me)
> Dreamin' Of You (sung by the popular Selena)
> I Dreamed A Dream
> Out Of My Dreams (and in to your arms).
>   Lyrics by Oscar Hammerstein, from "Oklahoma"

Modern poet John Berryman (1914-1972) received universal acclaim for his "The Dream Songs" (Pulitzer Prize, 1964), an expression of his lifelong struggles with literary creativity, alcoholism, sexual promiscuity, failed marriages, depression, and suicide attempts (finally successful in 1972, when he jumped off a bridge in Minneapolis). These poetic dream songs would have given Dr. Freud much to contemplate.

Compliments to Dr. Friedman for his interesting essay.

– **Melvin Hershkowitz, MD**

To the Editor,

I am sorry that you stifled your opinion on house officer dress codes in the face of your daughter's naïve idea of youthful feminist freedom. [January 2007] This is the precise situation in which the gray heads must stick to their guns.

Those of us actively engaged in teaching have a proprietary interest in the overall education of our medical students and residents. This includes professional appearance and behavior as much as how to do a physical exam or close an abdomen. Dress is as much a part of patient interaction as interviewing skills and empathy. I would be just as remiss allowing my charges to dress inappropriately on the wards as wearing street clothes in the OR.

The doctor-patient relationship is primarily one of extraordinary trust on the part of the patient. We must do everything in our power to make sure that the level of respect accorded our patients is not besmirched by some misguided paean to individual expression or the current modern fashion. We must lead by example and guidance, regardless of the discomfort it may bring.
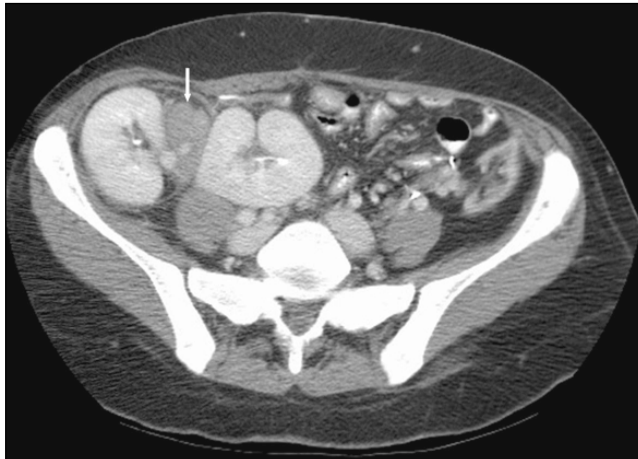
– **Stephen E Glinick, MD**

Images In Medicine

Post-transplant Lymphoproliferative Disorder Following Renal Transplant

Courtney A. Woodfield, MD

A 46 year-old male 8 months status post renal transplant for autosomal dominant polycystic kidney disease presented to the emergency department with fever and was found to have normal renal function. An enhanced CT examination of the abdomen and pelvis demonstrated a homogeneous soft tissue attenuation mass (arrow Figure 1) centered on the hilum and encasing the central vessels of a right lower quadrant double pediatric (en bloc) cadaveric transplant. Ultrasound guided percutaneous biopsy of the perinephric mass confirmed **post-transplant lymphoproliferative disorder (PTLD)**, polyclonal subtype. The patient was treated with decreased immunosuppression with subsequent mass regression on follow up CT imaging.

PTLD is a spectrum of lymphoid disorders resulting from immunosuppression after organ transplantation, ranging from B-cell hyperplasia to aggressive (usually B-cell) lymphoma. PTLD is associated with Ebstein-Barr virus infection of recipient B-cells with unopposed B-cell proliferation. Any nodal or extranodal site may be involved.[1]

Imaging plays an important role in the detection and diagnosis of PTLD as early lesions have a better prognosis and can often be managed with immunosuppression alone. More advanced PTLD lymphoma has a poorer prognosis with need for chemotherapy.

PTLD of the transplant kidney typically manifests as a hilar-centered mass or less commonly as a diffuse, low attenuation infiltrative process of the kidney. (Figure 2) Imaging evaluation of renal transplants usually begins with ultrasound which can depict PTLD as hypoechoic mass(es) adjacent to the transplant kidney. CT or MRI is useful for indeterminate ultrasound exams and for establishing the size and extent of disease. Figure 3 is an enhanced axial T1-weighted fat saturated MR image of renal transplant PTLD with enhancing soft tissue mass of the renal hilum (long arrow) encasing the right iliac vessels. The low signal transplant ureter is also dilated (short arrow).

CORRESPONDENCE

Courtney A. Woodfield, MD
Department of Diagnostic Imaging
Brown Medical School
e-mail:cwoodfield@lifespan.org

REFERENCES

1. Kew CE, Lopez-Ben R, et al. Postransplant lymphoproliferative disorder localized near the allograft in renal transplantation. *Transplantation* 2000;68:809-14.
2. Scarsbrook AF, Warakaulle DR, et al. Post-transplantation lymphoproliferative disorder. *Clin Radiol* 2005;60:47-55.
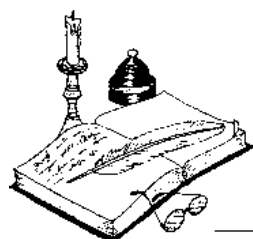
Physician's Lexicon
The Vocabulary of Paralysis in Anglo-Saxon England

Old English, the ancestor of the language we speak today, was first written down about thirteen hundred years ago by people we call the Anglo-Saxons. Surviving Old English texts from this period, including some medical leechbooks or *lǽcebocas*, are rich in terms associated with paralysis, many of which we hear echoed in our own speech and others which have fallen from the language or are scarcely recognizable. Although *paralysin*, a borrowing from Greek via Latin, occurs in some Old English texts, the most common term for paralysis was *lyftadl*, meaning weak disease. The first element of this word is derived from Old English *lef*, weak, and is related to our word for the weaker hand in those who are dextrals. (The right hand in Old English was the *swithere*, the stronger.) *Adl* had the general meaning of ailment or sickness, and

occurs in the vivid Old English expression for hemiplegia, *healfdead adl*. This is paralysis that comes "on the right half of the body or the left where the sinews are powerless," as one of the Anglo-Saxon leechbooks describes it. Old English *seonu*, sinew, was used indiscriminately for what are now called nerves, tendons and ligaments. In this the Anglo-Saxon authors differed little from their Latin models who used *nervus* in the same way.

That *lyftadl* could also include loss of sensation is reflected in other terms applied to a paralyzed part such as *aslapen* or *adeadod*, much as we might say a limb feels asleep or dead. These terms may also have been used for paralytic stroke, along with *aslegen*, which has the basic meaning of stricken and is an ancestor of our words slay and slain. One instance of Greek *apoplexia* is glossed by Old English

færdeath, sudden death, suggesting that treatment could often be futile, as Hippocrates had discerned. Paralysis might also leave one *spæcleas* or suffering from *dumbnes*, although this seems to have been blamed primarily on paralysis of the tongue, a very old and persistent notion. Depressed skull fracture following a blow to the *brægenpanne* could also cause one to go silent.

The prevailing explanation for paralysis, including *healfdead adl*, was that harmful humors, *yfel wæta*, clogged presumptive channels in the sinews by which the *brægen* communicated with the rest of the body and vice versa. Treatment was directed at removing the offending humors from the paralyzed part by application of healing *sealfas* and other plas-
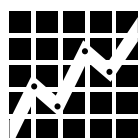
---

VITAL STATISTICS

Rhode Island Monthly Vital Statistics Report Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	March 2006	12 Months Ending with March 2006		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	249	2,757	257.7	4276.0
Malignant Neoplasms	189	2,281	213.2	6,364.0**
Cerebrovascular Diseases	41	446	41.7	680.0
Injuries (Accidents/Suicide/Homicide)	40	445	41.6	6,857.5
COPD	46	469	43.8	352.5

Vital Events	Reporting Period		
	September 2006	12 Months Ending with September 2006	
	Number	Number	Rates
Live Births	1,155	12,996	12.1*
Deaths	783	9,850	9.2*
Infant Deaths	(4)	(89)	6.8#
Neonatal Deaths	(2)	(70)	5.4#
Marriages	986	7,129	6.7*
Divorces	269	3,130	2.9*
Induced Terminations	433	4,792	368.7#
Spontaneous Fetal Deaths	86	921	70.9#
Under 20 weeks gestation	(71)	(862)	66.3#
20+ weeks gestation	(15)	(59)	4.5#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,069,725

(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

* Rates per 1,000 estimated population
\# Rates per 1,000 live births
** Excludes 2 deaths of unknown age

MEDICAL MALPRACTICE TOPICS

INFORMATION FOR RHODE ISLAND PHYSICIANS FROM BABCOCK & HELLIWELL

Plan for the Unexpected
Office Emergencies
John Tickner, CPCU, President, Babcock & Helliwell

With a busy medical practice it is easy to forget to prepare for office emergencies. However, you must anticipate and plan for any event that could cause injuries or disrupt your practice's ability to function.

Is your staff ready to respond quickly and properly if there's a fire, a bomb threat, or if a patient in the waiting area suffers cardiac arrest? What if medical records are accidentally or deliberately destroyed?

Training your office staff to respond effectively to any type of adverse event can reduce the likelihood of a claim being filed against you, and can help insure quality patient care. While it isn't practical or affordable to plan for every possible event, it takes relatively little time and money to anticipate the most common situations and to develop an office emergency plan.

Begin by determining the most likely emergencies that you could face. Include your staff when you're developing response plans, since flexibility and teamwork are crucial in an emergency situation. It will be easier to develop and carry out workable strategies with everyone on board. Then follow these steps:

- Identify potential crises and decide which to prepare for.
- Develop basic contingency plans.
- Procure needed resources.
- Train staff to carry out the plans, and reinforce the training with periodic drills.
- Post a list of emergency numbers, including the name and phone number of a key staff member available 24/7.
- Test your plans at least once every six months.

Many medical practices will have to deal with an in-office medical emergency. The immediate priority should be on giving clinical treatment and emotional support to those involved. While most staff members have the skills to deal with such an emergency, they must also know how to respond as a team. Assign staff members specific responsibilities. Make a list of who will:

- Call 911.
- Assess the condition of any injured individual and initiate CPR if needed.
- Pull the medical records of the injured person, if available.

- If the person is new to your practice, search their belongings for medical information or ask the person who brought him or her to the appointment.
- Escort other people out of the immediate area (if appropriate).

There are several things that you, the physician, will need to do when an emergency occurs:

- Stabilize the injured person.
- Talk to your staff about which facts can be ascertained and which remain unknown.
- Explain the known facts to the injured person and/or his or her family (if present) in non-technical language.
- Empathize with the injured individual and/or the family by acknowledging their shock and worry; admit your own concern as well.
- Do not blame *anyone* for the event.
- Remain calm, providing an example for your staff.

Whenever such an event takes place, fill out an incident report. Keep it on file to preserve the facts and to help identify, investigate, and correct problems. Again, be careful not to assign blame or document any opinions about the cause of the event. If the incident involves a patient, the report should *not* be included in the patient's file, nor should the file make any reference to it.

Don't discard any supplies and equipment that you suspect contributed to the incident. This could become vital evidence in future litigation; conversely, their absence could give the impression of a deliberate cover-up. Contact your insurance agent or company immediately after the event. They will probably have an expert evaluate the equipment and document the chain of custody of all items involved.

John Tickner, CPCU, is president of Babcock & Helliwell, a privately held independent insurance agency established in 1892 that provides professional insurance-related services of all kinds. Babcock & Helliwell is an agency for ProMutual Group, New England's largest medical malpractice insurance provider and the second-largest provider in Rhode Island.

Babcock & Helliwell
Insurance and Risk Management

Representing... **ProMutual**Group

138 Main Street, Wakefield, RI 02879   [tel] 401.782.1800   www.babcockhelliwell.com

NINETY YEARS AGO, MARCH 1917

In "A Study of Empyema or Pyothorax," John W. Keefe, MD, FACS, bemoaned the "lack of investigating interest on the part of the profession at large." He cited a high mortality, even "for this enlightened age." "The cases of so-called recovery with a deformed chest, a displaced heart, or a curved spine, an impaired function of lung or diaphragm, make the word 'recovery' a travesty."

In "Hookworm Disease in Rhode Island, Alex M. Burgess, MD, and Perry D. Meader, ScM, discussed the state's 8 diagnosed patients: 4 had lived in Providence for 2 years, 1 for 1 year, 2 had recently arrived, and 1 had probably lived in RI for at least 2 years, but had returned to his native Portugal. Because of the chilly winter temperatures, the authors were not concerned about contagion.

Harry S. Bernstein, MD, Consulting Pathologist, contributed "Case of Tuberculous Meningitis" [from the Medical Clinic of St. Joseph's Hospital]. A 14 year-old girl arrived at the hospital in a coma. Her medical history included whooping cough, measles at age 2, chicken pox at age 5, diphtheria at age 8, bronchitis at age 13. Ten days prior to admission, she felt drowsy and weak. Two days later, she complained of severe headaches. Soon afterward, she started vomiting, became incontinent. Three days after admission, she died. The physicians considered poliomyelitis and encephalitis in the differential diagnosis; a lumbar puncture excluded infections due to pyogenic organisms. To know the "character of the infection," the author inoculated 2 guinea pigs with a centrifugalized specimen of spinal fluid. The author concluded: "It is difficult to distinguish tuberculous meningitis from acute poliomyelitis …"

FIFTY YEARS AGO, MARCH 1957

Anthony V. Migliaccio, MD, and J. Robert Bowen, MD, in "Tears of the Mesentery," discussed 6 such patients treated at Rhode Island Hospital in the past 15 years. (One patient died.)

Anthony Carditi, MD, in "Rheumatic Carditis in late Adult Life," discussed 3 cases (ages 54, 64, and 70). He stressed the importance of early diagnosis: "…underlying atherosclerotic or inactive rheumative heart disease itself may confuse the clinical picture."

J. Merrill Gibson, Jr, MD, discussed "Breast Carcinoma with Pregnancy or Lactation," a rare occurrence (2% of breast cancer patients), with a poor prognosis (5-year survival 17%). The basic treatment was the same for patients, regardless of pregnancy: biopsy and radical mastectomy; but the decisions revolved around timing and termination. Five-year survivals almost doubled when the pregnancies were terminated.

An Editorial supported "chemical testing of motorists alleged to have driven vehicles while under the influence of alcohol." The Rhode Island Council on Highway Safety had introduced such legislation in the General Assembly.

TWENTY-FIVE YEAS AGO, MARCH 1982

In a "Current Commentary" column, Paul T. Welch, MD, asked readers to support "A Uniform Determination of Death Act." For the past five years, the General Assembly had shelved those bills.

Rebecca Silliman, MD, Mary Ann Passero, MD, David Kaplan, MD, Mary Condry, RN, Constance Pass, Philip Robzyk, Michael Passero, MD, contributed "Acute Cardio-respiratory Morbidity, Air Quality, Temperature and Pollen Concentration in RI." They cited the results from a study that suggested a relationship between air pollutants and temperature and the incidence of bronchospasm. The study sample included all patients admitted to Roger Williams General Hospital or treated as an outpatient with complaints of cardiopulmonary disease, during the warm months of 1980.

David H. Nichols, MD, FACS, FACOG, in "Clinical Pelvic Anatomy, the Types of Genital Prolapse and the Choice of Operation for Repair, " advised: "In most instances a transvaginal operation is indicated."

---

ters, while purging them from the entire body by a *clænsung*. The latter could be effected by an appropriate *blodlæting*, by provoking emesis with the aid of a *spiwdrenc*, or, if the face was involved, by drawing the *yfel wæta* from the head through the nose and mouth with special concoctions and causing the patient to sneeze, *gefnesan*.

Those left permanently impaired by paralysis and forced to hobble or pull themselves along the ground were called *creopere*, *crypel*, or, most evocatively, *eorthcrypel*, all words related semantically to the notion of creeping. The *lama* and the *healt* could perambulate with the aid of a *crycc* and included not only the partially paralyzed but those, for example, made *limleas* by traumatic injury. The most gravely impaired were the *beddridan*, destined to 'ride' their beds until freed by death or the intervention of a saint.

– **JAMES T. MCILWAIN, MD**

James T. McIlwain, MD, is Professor of Medical Science Emeritus, Brown Medical School.

Figure 1 in the article entitled "Biohybrid Limbs: New Materials and New Properties," (p.4) of the January 2007 issue was not credited. The scanning electron micrograph images were courtesy of J. Dennis Bobyn, PhD, Jo Miller Orthopaedic Research Laboratory, Montreal General Hospital, McGill University.

The Name of Choice in MRI

Open MRI
of New England, Inc.

- Open-Sided and 1.5 Tesla High Field Systems
- Fast appointments and reports
- Instant internet access to studies
- Locations in Cumberland, East Providence, North Smithfield, Providence, Warwick & Westerly

Open **MRI** *of New England, Inc.*

ADVANCED
Radiology, Inc.

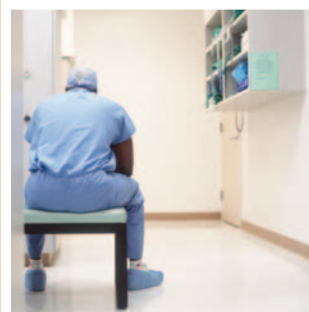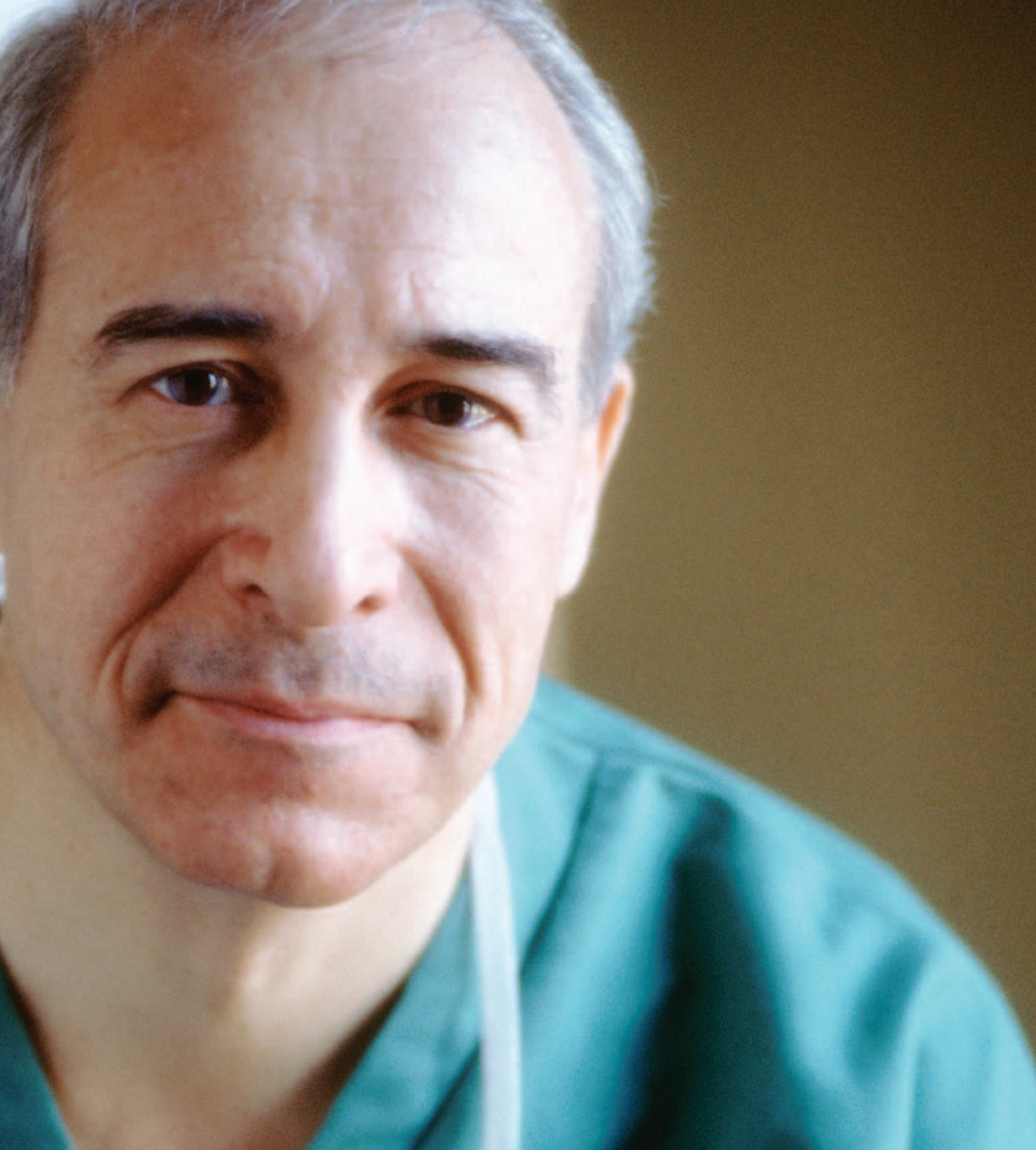- "Multislice" CT systems by GE
- Digital xray, bone density and ultrasound
- Fast appointments and reports
- Instant internet access to studies

AR ADVANCED *Radiology, Inc.*

525 Broad St • Cumberland
Tel. 725-OPEN (6736) Fax 726-2536

1002 Waterman Ave • East Providence	148 West River St. • Providence	501 Great Road • North Smithfield	335 Centerville Rd • Warwick	101 Airport Rd • Westerly
Tel 431-5200 Fax 431-5205	Tel. 621-5800 Fax 621-8300	Tel 766-3900 Fax 766-3906	Tel. 732-3205 Fax 732-3276	Tel 315-0095 Fax 315-0092