

The Center for Liver Disease & Transplantation

NewYork-Presbyterian Hospital
Columbia University Medical Center

Liver News *Winter 2009*

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The Center for Liver Disease and Transplantation Marks Its 1000th Liver Transplant

For the celebration of the center's 1000th liver transplant, clinical and administrative staff folded 1000 origami paper cranes.



On October 4, 2008, the Center for Liver Disease and Transplantation (CLDT) at NewYork-Presbyterian Hospital/Columbia University Medical Center performed its 1000th liver transplant, in a one-year-old girl. This milestone was the product of tireless dedication over many years and dedication of our entire staff: surgeons, hepatologists, diagnostic and pathology experts, nurse practitioners, social workers, psychiatrists, physician assistants, nurses, and administrative assistants.

The center celebrated the event on December 15, 2008, bringing together many of its transplant patients and reuniting them with the clinicians and staff who ushered them through the transplant and recovery processes. More than 200 of the center's patients were in attendance. The CLDT's first transplant took place, January 20, 1998, when Juliana Reed, now 10 years old, was transplanted with an organ donated by her father on the day of her first birthday. We are immensely proud of the fact that 10 years after receiving a new liver, many of our first liver transplant recipients continue to enjoy restored health. To mark the occasion, the team at the CLDT folded 1000 origami paper cranes, a gesture that, according to an ancient Japanese legend, entitles us to wish long

life or recovery from illness. This is our wish for each transplant recipient. And it is also our wish for the organ donors and their families, who give selflessly in order to save a life.

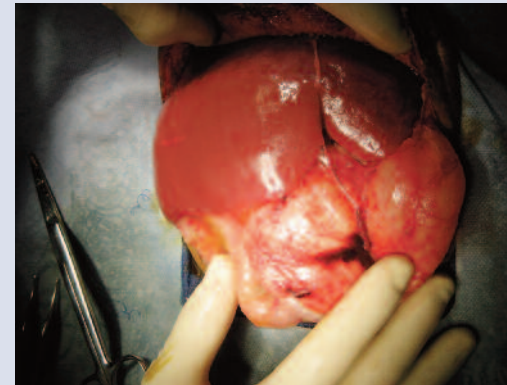
Exciting innovations are on the horizon that will affect future patients. We are in the midst of a major initiative to expand our liver program to include:

- expertise in multi-organ transplantation;
- a new surgical procedure called APOLT (auxiliary partial orthotopic liver transplantation), which enables us to resuscitate a failing liver by attaching to it a portion of a healthy liver;
- new approaches to immunosuppression designed to make immunosuppressant medications unnecessary; and
- new ways to utilize expanded criteria organs.

Among those with end-stage liver disease, over 17,000 patients in the United States wait for a donated liver every year, but fewer than 6,000 receive one, and about 1,800 people die while on the waiting list. At the CLDT, we continue to passionately pursue improved access to transplantation and improved quality of life. ■



Michael J. Goldstein, MD, Surgical Director of Pediatric Abdominal Transplantation, performed the center's 1000th transplant on one-year-old *Jurnee Swan*.



Jurnee's new liver, received from a deceased donor on the West Coast.



For the celebration of the center's 1000th liver transplant, clinical and administrative staff folded 1000 origami paper cranes.

Living Donor Transplants: A Survival Benefit for Recipients

Patients with cirrhosis and end-stage liver disease face many challenges to enjoying long and healthy lives.

Unfortunately, in New York State, worrying about organ availability is one of those challenges. Living donor liver transplantation is a valuable and proven option for the sickest of these patients.

Because the average MELD score for patients transplanted in Region 9 (New York and Vermont) is often above 30—which typically means significant kidney failure, bleeding problems, and jaundice—transplantation can mean waiting years while sick (MELD, short for Model for End-Stage Liver Disease, was developed by the United Network for Organ Sharing (UNOS) and gives the sickest patients priority for organ allocation.). For patients with liver cancer, waiting for MELD score to rise above 30 means living with cancer for more than a year and risking metastasis. In fact, while the average waiting time for deceased donor liver transplants is 14 months in the United States, it is more than 32 months in the New York region. Columbia researchers at New York-Presbyterian Hospital have shown that early transplantation of patients with complications of cirrhosis such as refractory ascites, encephalopathy, variceal bleeding, and liver cancer confers a survival benefit.

The Center for Liver Disease and Transplantation (CDLT) has offered patients living donor liver transplantation (LDLT) for more than a decade, providing them with earlier access to transplantation. The CDLT is one of the most experienced LDLT teams in the country, with more than 160 LDLTs performed at New York-Presbyterian Hospital/Columbia University Medical Center since 1998. Jean C. Emond, MD, Vice Chair for Transplantation at New York-Presbyterian Hospital/Columbia was part of the surgical team that pioneered this type of transplantation.

The key to the success of our LDLT program has been our commitment to the safety of all donors. Our development of an independent donor advocacy team (IDAT), which evaluates each



Mark Miller donated a portion of his liver to his sister, Sharon Lupo.

donor with a primary focus on the safety of the donor, has been central to that commitment.



Benjamin Samstein, MD
Assistant Professor of Surgery

For adult LDLT, the donor typically undergoes right lobe donation. While this requires removal of 50-65% of the liver, it quickly regenerates, with the donor's liver growing to greater than 90% of pre-donation size in eight weeks. For a pediatric LDLT, 20-25% of an adult donor's liver, the left lateral segment, is adequate for the procedure. Reviewing our experience with left lateral segment donation for pediatric recipients we found that all 48 donors have had outstanding outcomes. No donors required blood transfusions, only one donor developed a hernia, and no donors had significant biliary complications.

While donor safety is essential to a good outcome for any LDLT, it must be accompanied by excellent recipient outcomes as well. LDLT recipients at the CLDT have enjoyed a nearly 95% early graft survival. But most importantly, rates of long-term function and survival of our living donor recipients have been excellent. While recipients of LDLT in the United States have a three-year survival of 83%, this number is 88% at the CDLT. That figure is 10% higher than the three-year survival for deceased donor liver transplants in the United States.

Earlier transplantation, superb donor outcomes, and superior recipient results are why LDLT is an integral part of the options available to CLDT liver failure patients. ■

The CLDT living donor team is made up of clinical director Dianne LaPointe-Rudow, DNP, internist Doug Maratta, MD, social worker Anne Lawler, LCSW, psychiatrist Sylvia Haflinger, MD, and surgeon Benjamin Samstein, MD.

Sharing Expertise

During August 2008, Dr. Benjamin Samstein, live donor surgeon at the CLDT's Living Donor Liver Transplantation (LDLT) program, traveled to Asan Medical Center in Seoul, South Korea, whose liver transplant program, under the leadership of Sang G. Lee, MD, performs the highest volume of LDLTs in the world. During the past

year, Asan completed 250 LDLTs, including dual transplants and donor exchanges, or swaps. Dr. Samstein's 10-day visit included not only performing transplants, but participating in LDLT knowledge-exchange with Dr. Lee and Asan's team.

Hepatitis C Clinical Trials at the CLDT

GI and hepatology clinicians are familiar with the desperate need for new therapies to treat patients with hepatitis C (HCV), to help them avoid liver failure and ultimately liver transplant.

An added challenge is finding successful therapies without side effects. The Center for Liver Disease and Transplantation (CLDT) has focused clinical research addressing these issues since its inception. Our goal is to not only treat hepatitis at an early stage in order to prevent the need for transplant or the development of cancer but also to cure, prevent or ameliorate recurrent disease using treatments prior to or after transplant. Our research in this area has focused on the use of new antiviral therapies in hepatitis C as well as hepatitis B. We have participated in all of the trials of new HCV therapies including phase 2 through 4 studies of albumin interferon, as well as of telaprevir and boceprevir and other protease and polymerase inhibitors.

Access to these trials has provided patients with earlier access to groundbreaking treatments. We perform all trials in collaboration with referring physicians to ensure continuity of care is maintained and that procedures can be performed closer to home. This practice has yielded a higher level of patient compliance with medication regimens and has facilitated smooth management of adverse events. The result is higher rates of completion and sustained virological response. An overview of our recent, current, and planned trials follows.



Edward Eggleton, NP



Robert S. Brown, Jr., MD, MPH,
Director, Center for Liver
Disease and Transplantation;
Chief, Division of Abdominal
Transplantation

Trials In Process (closed to enrollment):

Achieve 2/3 — This phase 3 trial is evaluating the efficacy and safety of albumin interferon. This drug is given every two weeks for a period of 24 weeks, as opposed to the once-weekly standard therapy. It is used in combination with ribivirin for genotype 2 HCV patients.

Vertex 108 — A phase 3 trial comparing two different dosing regimens of telaprevir (a protease inhibitor). It is being used in combination with pegylated interferon alfa-2a and ribivirin in treatment-naïve subjects with HCV genotype 1.

Globimmune — A phase 2, randomized, open-label, multi-center therapeutic trial of the efficacy, immunogenicity, and safety of GI-5005. GI-5005 is an inactivated recombinant *Saccharomyces cerevisiae* expressing a HCV NS3-core fusion protein. This is given in combination with pegylated interferon plus ribivirin (standard of care) and is being compared to standard of care alone. Treatment is for patients with genotype 1 HCV.

Sprint — A phase 2 trial to test the safety and efficacy of the protease inhibitor boceprevir (SCH 5033034). This study is for subjects with chronic HCV genotype 1 who are previously untreated. Subjects are randomized to receive either boceprevir in combination with pegylated interferon plus ribavirin or pegylated interferon plus ribivirin only.

Upcoming Trials for Treatment-Naïve Patients

Sprint 2 Trial — This is a phase 3 trial using boceprevir plus ribavirin and pegylated interferon. This trial will be a double-blinded, placebo based, multi-arm study. The goals are to measure efficacy and duration of therapy.

Vertex 111 — A randomized study of stopping treatment at 24 weeks versus continuing treatment to 48 weeks in treatment-naïve subjects with genotype 1 chronic HCV who achieve an extended rapid viral response (eRVR) while receiving telaprevir, pegylated interferon alfa2a (Pegasys®), and ribivirin (Copegus®).

Non-Responder Trials

Respond 2 Trial — We are excited to be embarking on a trial for HCV patients who are nonresponsive to treatment or who relapse after treatment. This phase 3 trial will be using boceprevir in non-responders or relapsers. Major inclusion criteria will be genotype 1 patients who have been treated in the past with a 2 log drop in VL or who were VL negative and relapsed.

Pre-transplant Trial (still enrolling)

LADR Study — Because of evidence that cirrhotic patients undergoing liver transplant with an undetectable viral load will have better outcomes post liver transplant, new treatments are being evaluated. In this study, we are treating many HCV patients with traditional but decreased doses of pegylated interferon and ribivirin. We will be measuring safety and post-transplant outcomes.

Post-transplant Trial

PROTECT Study — We have just finished enrolling subjects for this aggressive multi-center study, using pegylated interferon and ribivirin in the post-transplant setting. Although this treatment has been the standard of care, it has yet to be officially studied. This study will offer us valuable outcomes data regarding its efficacy in our post-transplant patients ■

Advancing new therapies for liver disease and liver transplantation is central to the CLDT's mission, and our roster of clinical trials is continually changing. We invite physicians to contact us directly at 212-305-0914 about their patients with liver disease who might benefit from participating in a trial.

Acute Liver Failure: Proper Management and Timing of Referral Is Critical for Emergent Transplantation

Acute liver failure is defined as the onset of hepatic encephalopathy and coagulopathy within eight weeks of jaundice without pre-existing liver disease.



Sonja Olsen, MD, AASLD Fellow, Division of Digestive and Liver Diseases

Acute liver failure (ALF) is relatively rare, with about 2,000 cases per year in the United States. However, a mortality rate of 60-70% in the absence of transplantation underscores the need to refer the patient to a transplant center as soon as possible. If you suspect ALF, the time to refer a patient is before they develop any signs of encephalopathy. Since encephalopathy can develop quite rapidly, a conversation with a transplant center cannot occur too soon.

Survival is determined by the etiology of liver failure and by the stage at which the patient comes to medical attention. In the United States, the majority of ALF (> 50%) is due to acetaminophen toxicity. Patients with ALF from hepatitis B, from drug toxicity other than acetaminophen, or from unknown causes, are more likely to require transplantation than those with acetaminophen toxicity. While many criteria have been proposed to derive prognosis in ALF (King's College criteria,¹ APACHE II score,² and MELD score,³ to name a few), there is not enough data to recommend one particular scheme or laboratory value. Typically, the Center for Liver Disease and Transplantation (CLDT) relies on the MELD score. The poor prognosis and complexity of the disease underscore the paramount importance of referring the patient to a transplant center early in the disease course.

It is critical to understand the basic principles of managing a patient with acute liver failure. An overview of these principles follows.

- ALF should be considered more of a syndrome than a disease.
- In addition to running a battery of tests to determine the etiology of ALF, it is important to monitor the patient's mental status closely, to treat with N-acetylcysteine in the cases of acetaminophen toxicity, and to empirically administer vitamin K, although the coagulopathy of ALF is unlikely to resolve with this intervention.

- Patients will often develop renal failure and respiratory failure, and managing them requires input from several different subspecialty teams.
- Although infection is a leading cause of death in patients with ALF, there is little data that can help guide judicious use of antibiotics and antifungal therapy. Patients with ALF often manifest infections in atypical ways and are at increased risk of fungal infections.⁴ Most experts agree that empiric use of antibiotics is warranted when patients develop grade III encephalopathy,⁵ experience refractory hypotension, or manifest signs of systemic inflammatory response syndrome (SIRS).⁶
- Suppression of gastric acid with either H2 antagonists or proton pump inhibitors is also recommended as a method of reducing the incidence of upper gastrointestinal bleeding.⁷

One of the most frightening complications in the patient with ALF is the development of cerebral edema and resultant increased intracranial pressure. In fact, cerebral edema remains one of the major causes of death in patients with ALF.⁸ Although progression to Stage III or IV encephalopathy is certainly worrisome for cerebral edema, there is no physical exam-finding that can reliably enable us to detect intracranial pressure. CT scans are not adequate for its diagnosis.⁹ At NewYork-Presbyterian Hospital/Columbia University Medical Center, we have partnered with our neurology and neurosurgical colleagues to ensure that our patients with ALF are followed closely and that intracranial monitors are placed in a timely fashion in order to evaluate and regulate cerebral pressures if necessary. ■

ALF Trial News

Columbia researchers at NewYork-Presbyterian Hospital have recently received approval to study the use of an extracorporeal liver assist device (ELAD) for ALF patients as a bridge to either transplant or clinical improvement. The ELAD employs artificial hepatocytes placed on a membrane stored in a cartridge. The patient's plasma is passed through the membrane in order to clear the plasma of toxins that are normally filtered by the functioning liver. Studies are ongoing to evaluate the role and benefits of such liver replacement devices and to define the patient population that stands to derive maximum benefit.

¹O'Grady JG, Alexander GJ, Hayllar KM, et al: Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology* 1989; 97:439-445.

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⁴Rolando N, Harvey F, Brahm J, et al: Fungal Infection: A common, unrecognized complication of acute liver failure. *Journal of Hepatology* 1991; 12: 1-9.

⁵Vaquero J, Polson J, Chung C, et al: Infection and the progression of hepatic encephalopathy in acute liver failure. *Gastroenterology* 2003; 125:755-764.

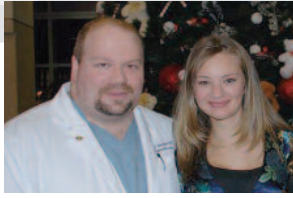
⁶Rolando N, Wade J, Davalos M, et al: The systemic inflammatory response syndrome in acute liver failure. *Hepatology* 2000; 32 (4 pt 1):734-739.

⁷MacDougall BR, Williams R: H2-receptor antagonist in the prevention of acute upper gastrointestinal hemorrhage in fulminant hepatic failure: A controlled trial. *Gastroenterology* 1978; 74 (2 Pt 2):464-465.

⁸Ware AJ, D'Agostino AN, Combes B: Cerebral edema: A major complication of massive hepatic necrosis. *Gastroenterology* 1971; 61:877-884.

⁹Munoz SJ, Robinson M, Northrup B, et al: Intracranial pressure monitoring and computed tomography of the brain in fulminant hepatocellular failure. *Hepatology* 1992; 16: 1-7.

Case Study: Immediate Referral to Transplant Saves a Life



James Guarrera, MD, successfully transplanted Krista Lesinski's failing liver.

Eight weeks prior to admission to the Center for Liver Disease and Transplantation (CLDT) for evaluation, immediate UNOS listing, and liver transplantation, a 22-year-old-female with no significant past medical, surgical, or family history had an episode of acute sinusitis, bilateral lower extremity edema, and facial rash. Over the

ensuing weeks, she progressively felt worse but did not seek medical attention until becoming acutely jaundiced with abdominal distension and hematochezia.

DAYS 1-2 Having experienced abdominal distension and hematochezia for three days, the patient presented to a local hospital with fever, creatinine 2.3, INR 4.2, total bilirubin 19, WBC 23,000 (5% bands), and elevated LDH. A diagnosis of Wilson's disease was considered and an ophthalmologist was called. Examination revealed Kayser-Fleischer rings, which nearly always confirms a diagnosis of Wilson's disease. She had no family history of liver disease and no prodrome of neuropsychiatric symptoms. She denied ingestion of herbal supplements or over-the-counter medication. She had no history of ETOH (ethanol) abuse. She was treated symptomatically, started on broad spectrum antibiotics, and referred to The Center for Liver Disease and Transplantation (CLDT) for liver transplant evaluation.

DAY 3 The patient arrived at the CLDT and was admitted to the medical intensive care unit with total bilirubin 44.9, INR 4.92, AST 241, ALT 17, creatinine 5-7, and ammonia level 103 with asterixis. An expedited transplant evaluation was commenced. Imaging of the liver was ordered. In addition, she was evaluated for a determination of the etiology of acute liver failure, including evaluation of: copper and ceruloplasmin levels for Wilson's disease (Kayser Fleischer rings, AST > ALT

with low alk phos, autoimmune hemolytic anemia); serum porphyrins to determine hepatic porphyria (skin findings, hematochezia prodrome); anti-smooth muscle antibody and ANA for evaluation of autoimmune etiology; and viral hepatitis serologies. Results were negative except for confirmation of the Kayser Fleischer rings, copper 365, and ceruloplasmin 24.

DAY 4 Expedited transplant evaluation was completed, and patient was listed with UNOS as a Status I candidate (priority status). The patient became more somnolent and was intubated for airway protection. She became hemodynamically unstable, requiring vasopressors. A vascath was inserted and continuous veno-venous hemodiafiltration was begun. A head CT was performed in order to rule out cerebral edema; the scan was normal. The team set short-term goals of continuing aggressive management, vasopressor agents, blood products as needed, consideration of repeat head CT scans to monitor for cerebral edema, and labs every four hours.

DAYS 4-5 The patient remained critically ill, unresponsive and hemodynamically unstable. An appropriate organ was allocated by UNOS and the patient underwent emergent liver transplantation.

DAY 5 The pathology of the hepatectomy confirmed the diagnosis of fulminant Wilson's disease. The patient was managed postoperatively with supportive therapy and the center's standard post-transplant antirejection and antibiotic therapy. Her renal failure resolved after one month. She was hospitalized for six weeks.

Timely referral to our transplant center, aggressive management of this patient, and collaborative efforts of our referring physician and our transplant team resulted in a successful outcome. The young woman is alive and has made a full recovery and lives with her family in New York State. ■

Call early to begin the transplant process. Obtaining insurance clearance and finding the appropriate hospital setting can take time. Every hour is important and can make the difference between a poor outcome and a successful transplant.

Center for Liver Disease and Transplantation at NewYork-Presbyterian Hospital/Columbia

Adult Liver Transplant Program Clinical Faculty and Staff

Referrals: 212-305-0914 Physician on call: 212-305-0914 Fellow on call: 212-305-5880, pager 89666. We are available 24 hours a day, 7 days a week.

Columbia Office:	212-305-0914	Transplantation Psychiatrists		Pharmacist:	
Weill Cornell Office:	646-962-4129	Sylvia Hafliger, MD	212-342-2787	Anastasia Balducci, PharmD	212-305-3292
Surgeons:		Lucy Epstein, MD	212-342-2786	Physician Assistants:	
Jean C. Emond, MD	212-305-9691	Clinical Staff:		Sonia Alford, PA	pager 84042*
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		Lourdes Matias, RN	646-962-4129	Nick Ginzburg:	212-305-2178

* Call 212-305-5880 to enter pager number.

To be added to our mailing list, please call 800-543-2782.

Treating an Emerging Menace: Nonalcoholic Fatty Liver Disease

Nonalcoholic fatty liver disease, which ranges from clinically insignificant steatosis to nonalcoholic steatohepatitis culminating in cirrhosis, is likely underdiagnosed and can be a cofactor in more commonly diagnosed chronic liver disease such as viral hepatitis.

Although the exact representation of nonalcoholic fatty liver disease (NAFLD) within the burden of liver disease is not known, and a minority of patients transplanted have a sole diagnosis of NAFLD, it has been estimated that a significant proportion of patients transplanted without a known etiology of cirrhosis had NAFLD as the cause of their cirrhosis. Steatosis is particularly dangerous to people with undiagnosed hepatitis because it can act as an ideal substrate for free-radical induced liver damage from hepatitis. The progression is undetectable at first: these patients may progress from simple steatosis with benign liver chemistry abnormalities to full blown hepatitis to cirrhosis.

NAFLD represents the hepatic manifestation of metabolic syndrome, or syndrome X as it is sometimes known. Metabolic syndrome involves hyperlipidemia, insulin resistance, and obesity, and may lead to damage in the vascular passageways of the heart and peripheral circulation. This same syndrome of lipid buildup ultimately results in damage to the liver. Prevention of progression of NAFLD from nonalcoholic steatohepatitis (NASH) to cirrhosis is the goal of therapy. Regrettably, therapy in the past has been mostly limited to weight loss and control of other features of metabolic syndrome. Weight reduction and diet modification remain the mainstay of treatment of the patient with metabolic syndrome. Patients will often show regression of their disease with modest weight reduction. Intensive lipid and glucose management also feature prominently in the care of the NAFLD patient, although there is little data suggesting that better glucose and lipid control will lead to true regression of NASH. New therapies are emerging to control NAFLD. Recently,

much interest has been focused on the use of insulin sensitizers. Pilot studies using PPAR-gamma agonists such as pioglitazone have shown improvement in liver chemistries and histology in NAFLD patients. Antifibrotic agents are in development to arrest the advent of fibrosis in NASH patients. The Center for Liver Disease and Transplantation (CLDT) is involved in clinical trials of novel agents to treat NAFLD and anticipates continued participation in this exciting work.

Fortunately, pharmacotherapy of NAFLD is beginning to emerge. Peroxisome proliferator-activated receptor agonists are a class of medications acting on skeletal muscle receptors to increase insulin sensitivity. This class of medications, which includes the drugs rosiglitazone and pioglitazone, has been shown to reduce transaminase levels to normal in small group of patients. Metformin has also been shown to have a benefit. These medications are currently the focus of larger trials to determine if these encouraging results can be translated to the population as a whole. Newer classes of medications targeting the liver directly are also entering clinical trials.

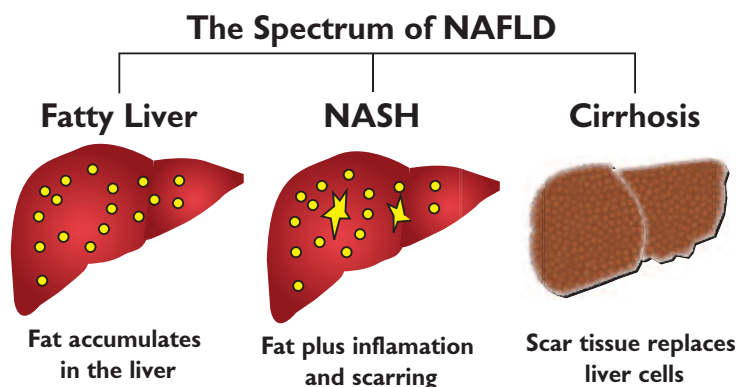


Scott Fink, MD, MPH, Assistant Professor of Clinical Medicine (in Surgery), transplant hepatologist

The ever-expanding waistline of the average American has most hepatologists convinced that we are just seeing the tip of the iceberg with regard to the representation of NAFLD within the overall burden of liver disease. Patients who are obese and have NAFLD may have survival and complication rates equivalent to those transplanted for other causes, provided their cardiovascular screening reveals them to be otherwise healthy.

If rising rates of heart and peripheral vascular disease are any clue, NAFLD will be a major cause of cirrhosis in the future.

The CLDT is taking a leadership role in the treatment of the patient with NAFLD. In the near future we will begin medication clinical trials to treat NAFLD. Our collaboration with Columbia University Medical Center's renowned lipid research teams is generating new ways of examining and treating the patient with NAFLD. ■



Psychiatry 101: Patients with End-Stage Liver Disease

Many patients with end-stage liver disease suffer from co-morbid depression, bipolar illness, and drug/alcohol dependency.



*Silvia Hafliker, MD
Assistant Professor of
Clinical Psychiatry*

In founding the liver transplant program at Columbia Presbyterian Hospital (now NewYork-Presbyterian Hospital/Columbia University Medical Center) with a vision of integrated psychiatric care, Drs. Jean Emond and Robert Brown set in motion a care system that would make a vast difference in quality of life for patients and their families. Obtaining psychiatric care in the community can be difficult, and at times almost impossible for these challenging and medically complex patients. Appointing a psychiatrist as part of the care team builds in improved medication compliance, decreases drug and alcohol abuse recidivism, and reduces the number of patients with debilitating neuropsychiatric side effects of interferon treatment.

Aside from the fact that depression in patients with liver disease is often not recognized, providers may undertreat these patients for fear of harming the liver. However, treatment with selective serotonin inhibitors (SSRIs) is not only safe for patients with liver disease, but it is quite effective. Below are general guidelines for treating depression in patients with advanced liver disease. It is best for these patients to include a psychiatric clinician in their comprehensive liver care. The Center for Liver Disease and Transplantation (CLDT) recommends citalopram, escitalopram, sertraline or venlafaxine for its patients. If patients can tolerate other medically indicated pills, they can tolerate antidepressants. Fluoxetine or paroxetine are less desirable because both are potent CYP2D6 P450 enzyme blockers, thereby prolonging metabolism of beta-blockers and many other medications. Fluoxetine has a very long half-life making it difficult to adjust to if patients have intolerable side effects. Paroxetine's half-life is less than 24 hours, and withdrawal symptoms such as diarrhea, flu symptoms, and rebound anxiety will occur if the drug is abruptly discontinued.

The key to starting a SSRI in a medically ill patient is to start low and go slow. Our recommended daily starting-doses are sertraline at 12.5 mg, escitalopram at 2.5 mg, citalopram at 5 mg, and venlafaxine at 37.5 mg. The medication is increased every seven days to prevent common side effects such as diarrhea, nausea, somnolence, headache, or anxiety. A good strategy for gauging whether the medication is effective is to work with the patient to select three target symptoms for monitoring. For example, the patient is improved if he or she cries less, sleeps better, socializes more, spends less time in bed, etc.

Patients with liver disease are likely to be reluctant to be treated with an antidepressant due to stigma, fear of addiction, or the responsibility posed by the medication regimen. To ensure compliance, family participation and discussion of potential side effects before initiating treatment is invaluable. Patients need to be reassured that there is no chance of drug dependency or addiction to an antidepressant, that treatment will not change their personality, and that their liver functions will not worsen. It takes 4-6 weeks to see the effects of antidepressants. If SSRIs are used for interferon-induced irritability or depression, treatment response can occur as early as two weeks.

If a patient's symptoms worsen with antidepressant therapy, bipolar illness should be considered. Patients may present with increased irritability, anxiety, or worsening of depression. It is important to obtain a thorough history about mood swings and family history of possible bipolar disorder before starting treatment with an antidepressant. If bipolar illness is suspected, we recommend tapering off the antidepressant and starting a mood stabilizer such as divalproex sodium, lamotrigine or an atypical neuroleptic such as quetiapine. Referral to a psychiatrist would also be in order as these patients pose treatment challenges.

Insomnia is a frequent complaint in patients with cirrhosis. Hepatic encephalopathy (a form of delirium) often presents with night/day reversal—a need to sleep late into the afternoon, and an inability to sleep at night. It can also present with symptoms of confusion, aggression, personality changes, and ataxia. Treatment with hypnotics such as zolpidem, eszopiclone or temazepam will often worsen this delirium. An effective treatment is low-dose quetiapine, 12.5 mg at bedtime, gradually titrated upward until the patient is able to fall asleep at bedtime. Usual doses for sleep are 50 to 100 mg of quetiapine. Other safe strategies include deseryl 25-100 mg or mirtazapine 7.5 to 15 mg to help with sleep.

Many patients referred to us for liver transplant are enrolled in a methadone program. We do not recommend stopping the methadone for these patients. Research has shown that 80-90% of patients who withdraw from methadone at a time of increased stress—such as referral for liver transplant—will relapse due to prolonged opioid withdrawal. In a liver transplant setting, relapse makes them ineligible for transplant. We recommend that providers taper the methadone to the lowest effective dose to prevent worsening of hepatic encephalopathy and relapse to opioid use.

Methadone is used in our program for pain management, as it has a long half-life and less abuse potential than oxycodone or dilaudid. If methadone is used for pain the dose has to be given every six hours, for example, 5 mg qid. Prevention of constipation in the setting of opioid use is essential, and before initiating methadone, a baseline EKG is recommended to watch for prolonged QTc syndrome.

Tobacco cessation is required in patients considered for transplant. Nicotine replacement strategies are offered to all our patients. Patients may use the a nicotine replacement patch or gum if cravings arise. varenicline has been used with some success, but vivid dreams, nausea/vomiting, insomnia, and irritability have been noted.

The CLDT is committed to a multidisciplinary approach to care and believes that managing addiction and psychiatric disease is the key to successful, long-term survival post-transplant. We provide services to assist patients and local providers to successfully managing these issues in our patients. ■

Announcing New CLDT Faculty



Tomoaki Kato, MD

Assistant Professor of Surgery, Columbia University College of Physicians and Surgeons
Surgical Director, Liver and Gastrointestinal Transplantation, Attending Surgeon,
NewYork-Presbyterian Hospital/
Columbia University Medical Center

A world-renowned specialist in multiple-organ transplantation, pediatric transplantation, and liver transplantation for adults and children, Tomoaki Kato, MD, has been appointed Surgical Director of Liver and Gastrointestinal Transplantation at NewYork-Presbyterian Hospital/Columbia University Medical Center and Assistant Professor of Surgery at Columbia University College of Physicians and Surgeons.

Previously Director of Pediatric Liver and Gastrointestinal Transplant and Professor of Clinical Surgery at the University of Miami School of Medicine, Dr. Kato is known for unique and innovative surgeries for adults and children, including six-organ transplantation; a liver transplant procedure called APOLT (auxiliary partial orthotopic liver transplantation) that resuscitates a failing liver by attaching a partial donor liver; making immunosuppressant drugs unnecessary over time; and the first successful human partial bladder transplantation, involving transplant of two kidneys together with ureters connected to a patch of the donor bladder. This March, in a highly publicized case, he led the first reported removal and re-implantation, or auto-transplantation, of six organs in order to excise a hard-to-reach abdominal tumor.

“Dr. Kato’s appointment represents an important part of our strategic transplant initiative, which will involve recruiting the nation’s top



Pedro Rodrigo Sandoval, MD

Instructor in Clinical Surgery,
Columbia University College
of Physicians and Surgeons
Attending Surgeon,
NewYork-Presbyterian Hospital

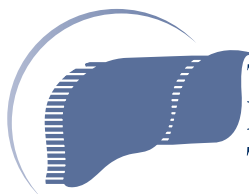
A graduate of Central University of Ecuador Faculty of Medical Sciences in Quito, Rodrigo Sandoval, MD, conducted his internship at

experts and expanding our research efforts—all with the aim of giving patients the best possible treatment options,” says Dr. Jean Emond, Vice Chair for Transplantation at NewYork-Presbyterian Hospital/Columbia University Medical Center.

A native of Tokyo, Dr. Kato received his medical degree from the Osaka University Medical School in Japan. He received his residency training in surgery at Osaka University Hospital and Itami City Hospital in Hyogo, Japan. He completed a clinical fellowship in transplantation at the University of Miami/Jackson Memorial Hospital, where he was subsequently appointed to the surgical faculty in 1997, and promoted to full professor in 2007. He served as a surgeon and senior leader of the liver and transplantation center at Miami’s Jackson Memorial Hospital, beginning in 1997, and at the University of Miami Hospital (previously Cedars Medical Center), beginning in 2004.

He is a member of numerous professional and honorary organizations, including American Society for Transplant Surgeons, American Gastroenterological Association, Transplant Society, International Pediatric Transplant Association, Society of University Surgeons, Japan Surgical Society, Japanese Society of Gastroenterological Surgery and Japan Society of Cancer Chemotherapy. He served on the United Network for Organ Sharing (UNOS) pediatric committee in 2005 and 2006 and has authored or co-authored more than 180 scientific papers in peer reviewed journals. Dr. Kato has been actively involved in promoting organ transplant in Japan, publishing two books for the lay public and appearing in a number of Japanese television documentaries. He is also helping to establish transplant services for children in underserved countries where transplantation is not widely available. ■

the Ecuadorian Institute of Social Security Hospital, also in Quito. He completed his general surgery residency at Case Western Reserve University in Cleveland, and completed a multi-organ transplant fellowship at NewYork-Presbyterian Hospital/Columbia University Medical Center. Dr. Sandoval’s clinical specialties include liver transplantation, laparoscopic and open hepatobiliary surgery, pancreas surgery, kidney transplantation, cross-match transplantation, laparoscopic donor nephrectomy surgery, and pediatric transplantation including kidney, liver, and small bowel. ■



**The Center for
Liver Disease &
Transplantation**

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