

## Some High-risk Donor Lungs Equivalent to Nonhigh-Risk in Transplant Outcome

*from Medscape Medical News*

The use of high-risk donors for lung transplantation results in good outcomes and would help mitigate the current organ shortage, according to Duke University investigators who described their experience April 22, 2010 at the International Society for Heart & Lung Transplantation 30th Anniversary Meeting.

In 2009, there were 1661 lung transplants performed in the United States and an inadequate number of donor organs to meet the demand. More than 10% of transplant candidates die on the waiting list each year, according to Shannon Novosad, MD, from Duke University in Durham, North Carolina, who presented the findings. “There is a clear need for ways to expand the donor pool, to utilize the current pool better, and to decrease the risk of death prior to lung transplant,” she said.

The Centers for Disease Control and Prevention (CDC) defines high-risk donors as people with relevant behavioral risk factors or exposure to HIV-infected people, inmates of correctional systems, and people with hemophilia. Nearly 9% of cadaveric solid organ donors are classified as high risk. Historic evidence has shown that the risk for disease transmission is less than 1% in seronegative donors; however, concerns arose in 2007 as a result of a high-profile transmission event. HIV and hepatitis C were transmitted to four recipients from a common donor who had tested negative at the time of donation. This was the only confirmed case of HIV transmission in more than 20 years.

“Surveys have shown that the majority of lung-transplant programs do not use high-risk donors,” Dr. Novosad said. She cited information from 11 centers showing only 18% accept an organ from any high-risk donor. The acceptance rates were 9% from men who have sex with men, 19% from intravenous drug users, 9% from prostitutes, 27% from any inmate, and 0% from current inmates; 64% accepted organs from people with tattoos.

“We hypothesized that high-risk donors may actually have more characteristics associated with good outcomes, such as younger age and better gas exchange, and that recipients of these lungs would have at least equivalent outcomes, compared with those receiving lungs from nonhigh-risk donors,” she said. The study was a retrospective review of the 186 lung transplants in the Duke database that were performed from 2004 to 2007; 166 were from nonhigh-risk donors and 20 were from high-risk donors. It also included a review of 12,576 transplants registered from 2005 to 2009 with the United Network for Organ Sharing (UNOS).

Investigators determined that 10.7% of lung transplants at Duke were from high-risk donors, as were 7.8% from the UNOS database. At Duke, 95% of potential recipients indicated that they would accept an organ from a high-risk donor, she noted. In the Duke experience, there was no significant difference in donor age

between high-risk and nonhigh-risk donors, but in the UNOS registry, high-risk donors were significantly younger than nonhigh-risk donors (age, 35 vs. 40 years;  $P < .0001$ ). In both databases, donor partial pressure of arterial oxygen was higher in high-risk than in nonhigh-risk donors ( $P < .0001$  for UNOS and  $P = .011$  for Duke). In the Duke cohort, high-risk donors were more likely to have a history of tobacco use (40% vs. 19.7%). The recipient characteristics between these groups were similar.

### Survival Better in High-Risk Donors

Interestingly, Duke recipients of high-risk donor lungs had better survival at 6 months than recipients of nonhigh-risk donors (100% vs. 85% and vs. 77% for the UNOS database). Their resource utilization was also lower, including mean hospital stay (19 vs. 27 days) and need for tracheostomy (27% vs. 10%). “We test patients at 3, 6, and 12 months for both hepatitis C and HIV, and there has been no transmission,” she added. “Our conclusion is that the use of high-risk donors by CDC criteria appears to be safe, and clinical outcomes are at least equal to recipients of nonhigh-risk donor lungs,” Dr. Novosad said. The group projected that increased use of high-risk donors would expand the lung donor pool by nearly 10%.

Session moderator Duane Davis, MD, professor of surgery at Duke, who was not involved in the current study, elaborated on the use of high-risk donors. “We don’t rule out high-risk donors. If the quality of the organ is acceptable and the recipient is at high risk, we don’t consider this an issue. We use the lung. Period,” he said, but he acknowledged that many centers are not so accepting. “The survey Dr. Novosad alluded to showed high variability, with only 18% actually using high-risk donors,” he noted, in spite of the Duke series showing that the overall quality of the organ was even better in the high-risk donor. Dr. Davis said he considers the use of high-risk donors a “risk/benefit issue” in which the risk of dying one year after lung transplantation is approximately 15% and the risk of contracting HIV or hepatitis C from a seronegative donor is “on the order of 1 in 1000 or more,” he pointed out.

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## Survival in Severe Alpha-1 Antitrypsin Deficiency (PiZZ)

Tanash HA, Nilsson PM, Nilsson JA, Piitulainen E., *Respir Res.* 2010 Apr 26; 11(1):44.

**Abstract:** Previous studies of the natural history of alpha-1-antitrypsin (AAT) deficiency were mostly based on highly selected patients. The aim of this study was to analyze the mortality of PiZZ individuals.

**Methods:** Data from 1339 adult PiZZ individuals from the Swedish National AAT Deficiency Registry, followed from 1991 to 2008, were analyzed. Forty-three percent of these individuals were identified by respiratory symptoms (respiratory cases), 32% by liver diseases and other diseases (non-respiratory cases) and 25% by screening (screened cases). Smoking status was divided into two groups: smokers 737 (55%) and 602 (45%) never-smokers.

**Results:** During the follow-up 315 individuals (24%) died. The standardized mortality rate (SMR) for respiratory cases was 4.70 (95% Confidence Interval (CI) 4.10-5.40), 3.0 (95%CI 2.35-3.70) for the non-respiratory cases and 2.30 (95% CI 1.46-3.46) for the screened cases. The smokers had a higher mortality risk than never-smokers, with a SMR of 4.80 (95%CI 4.20-5.50) for the smokers and 2.80(95%CI 2.30-3.40) for the never-smokers. The Rate Ratio (RR) was 1.70 (95% CI 1.35-2.20). Also among the screened cases, the mortality risk for the smokers was significantly higher than in the general Swedish population (SMR 3.40 (95% CI 1.98-5.40)).

**Conclusion:** Smokers with severe AAT deficiency, irrespective of mode of identification, have a significantly higher mortality risk than the general Swedish population.

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## Current Book Selections

*To the Edge and Back*, Chris Klug with Steve Jackson: My story from organ transplant survivor to Olympic snowboarder.  
*Heroes of My Transplant*, Allen Russell: After his successful transplant, Allen penned this book in the hope of relating to others the tranquility and peace he has gained through his journey.

*Liver Transplant; A 3-in-1 Medical Reference, Medical Dictionary, Bibliography & Annotated Research Guide to Internet Resources*, James N. Parker M.D. and Phillip M. Parker, PH.D. Editors: This collection of resources offers reputable websites and research education as well as recommended further discovery.

*Blow the House Down*, Charles Tolchin: The story of my double lung transplant (CF patient)

*Lung Transplant, A 3-in-1 Medical Reference; Medical Dictionary, Bibliography & Annotated Research Guide to Internet Resources*, James N. Parker M.D. and Phillip M. Parker, PH.D. Editors: This collection of resources offers reputable websites and research education as well as recommended further discovery.

*Organ Transplants*, Robert Finn: Making the most of your gift of life. Chapters go from considering transplant to the drugs, goes over most transplants, financial issues, Emotional responses, waiting, traveling for transplant, children.

*Organ Transplants—At Issue*, Susan C. Hunnicutt, Editor: Thirteen editorial type articles. Topics include: The need for donors, organ donation systems, criteria for defining donors, oversight of the US Transplant system, animal to human transplants, payment to donors.

*The Puzzle People*, Thomas E. Starzl: Memoirs of a transplant surgeon- the shaping and development of the transplantation system as we know it.

*Organ Transplants—It Happened to Me*, Tina Schwartz: A survival guide for the entire family- The ultimate teen guide.

*Life and Breath*, Neil Schachter, M.D.: The breakthrough guide to the latest strategies for fighting asthma, emphysema, and chronic bronchitis—at any age.

## Help Alhapatamus:

Find the words, which are forward, backwards, up, down, or diagonal.

BARBEQUE	J B F U V A C A M P I K K G
BASEBALL	S T A R G A Z I N G W L O D
BICYCLE	I E M R I X C A N O E D Y Q
BOOKS	E L L A B E S A B C K W H J
CAMP	Y I E C R E N E T N I A P W
CANOE	P B M X Y B Q D M I H P W L
EXERCISE	N R O O E C L U S A O M G U
FISHING	C A N B O R I E E P G N B Q
FRIENDS	S R A D G M C B S E I V O M
GAMES	J Y D N A T D I T H J N O I
GARDEN	T B E A R Q C A S H T N K W
HIKE	L B Y S D L K I T E V J S S
HOBBY	Z O H A E S F G E Z O S Z O
LEMONADE	R H C U N R A I P Y Z A V Z
LIBRARY	
MARBLE	
MOVIES	
PAINT	
PETS	
PICNIC	
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SANDBOX	
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Thank you for supporting Alphas through the work of the Alpha-1 Advocacy Alliance.

## Becoming Normal

by Ann Marie Benzinger



It was so nice moving around without oxygen tubing dangling from my ears. While I moved around in the house unassisted, I still needed the stability of the walker when I walked outside in the yard or for any distances. It was now August and I began to realize that once again, I was going to have a life; a life unattached to an oxygen tank and able to go places on my own with limitations. By the end of August, I was venturing out to the grocery

store making small purchases so that I would be able to bring them in to the house from the car all on my own.

In September, I began going back to the gym. I began slowly with the treadmill and the bike and slowly added time each day to increase my exercise limits. I added in light weights for my arms and upper torso. The clam shell incision that I had for the bilateral transplant had basically made the upper body muscles useless. I had to build them back up and teach them to work again. I had worked out a lot prior to transplant and my upper body was strong and muscular. My breasts didn't sag before, but now I had to look at my waistline to find the little things. (you can laugh here!) I had never understood the jokes women made about sagging breasts, but now I knew why. It would take months of weight lifting to begin to see improvement in that area.

By October I was driving my car and feeling very independent. I made my trips to the gym on a regular basis but I still felt weakness in my legs. I felt wobbly at times and so I was very careful to watch my steps. One Sunday upon returning from an outing, I stumbled on my sidewalk, tried to catch myself from falling on the brick only to fall in the grass. I bruised my knee and of course my dignity, but I got over that quickly. Less than a week later, I did the same thing only this time I was alone and carrying three bags of groceries. This time my arm hit the sidewalk in two places and ripped the skin open down to the ligaments. I had a difficult time trying to get myself up off the ground so I crawled until I could pull myself up on a chair. I then called my daughter to take me to the ER for stitches. This was my reality check. I was not normal, but I was getting there.

Medically at this time, the stent had to be dilated multiple times and twice lasered to basically clean out the overgrowth of tissue and mucus that accumulated in it. The procedures are painless because you are given anesthesia and numbing meds. One of my children has always taken me to these appointments as you are not allowed to drive following the procedure. My lab work was done periodically to check the cyclosporine levels and to look for any adverse numbers with my kidneys or blood. My pulmonary function tests were continually improving and all seemed well.

November and December found me able to celebrate the holidays with my family as my strength continued to improve. The Valcyte and Voriconazole (VFend) were discontinued so my med list got smaller. January found me not feeling well and wheezing. A bronchoscopy revealed my first bout of acute rejection. I checked into the hospital for a three day visit with large doses of solumedrol to treat the rejection. I was also started on

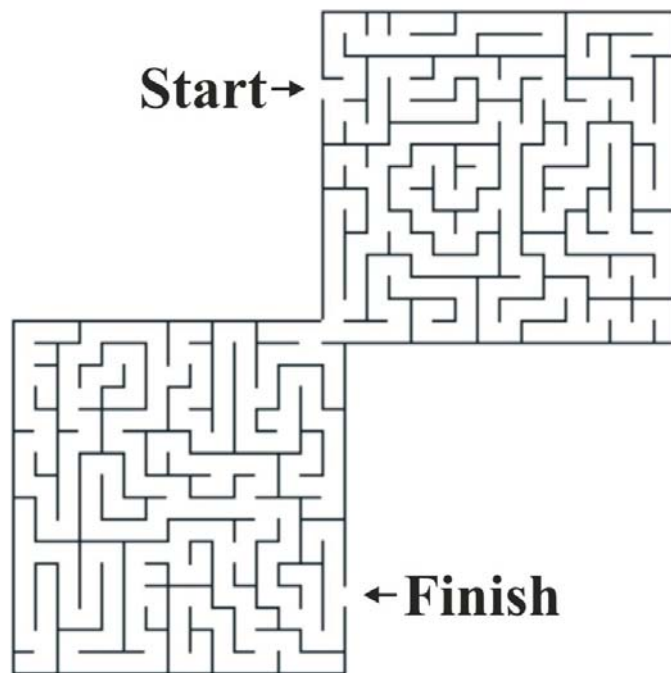
Rapamune, another anti-rejection drug which also helps restrict the growth of tissue within the airways that I was experiencing as well as aid in rejection. Blood work was performed more frequently to follow the levels of both anti-rejection drugs. A follow up bronc in February revealed the aspergillosis virus active in the lung so I had to re-start the VFend but there was no further evidence of rejection. At one point, blood work revealed my level of Rapamune too high, so the coordinator had me discontinue my dose completely.

Time marched on and the wheezing continued with no explanation. The bronchoscopies with bronchial lavage would give me immediate relief each time but it would not last more than a few days. The wheezing could be felt in my chest and I was unable to clear anything with coughing. Another bronc in April again revealed acute rejection but no aspergillosis in the lungs. My PFT's showed a slight decrease but nothing remarkable. The VFend was discontinued, another three day stay in the hospital getting solumedrol and I was started back on the Rapamune.

This was not quite what I had in mind for normal. While breathing is so much improved, challenges were beginning to make me question if I would ever return to what I felt was normal and resume a productive private life.

### Next: Complications and Dealing.

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A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
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## In Reporting Symptoms, Don't Patients Know Best?

By Denise Grady,

[http://topics.nytimes.com/top/reference/timestopics/people/g/denise\\_grady/index.html?inline=nyt-per](http://topics.nytimes.com/top/reference/timestopics/people/g/denise_grady/index.html?inline=nyt-per),

published: April 12, 2010; a version of this article

appeared in print on April 13, 2010, on page D1 of the New York edition.

About six years ago, my doctor gave me some samples of a drug to treat pain from an injury. I took it for a few days and then woke up one morning with a big red blister on my tongue. I'd never had anything like it before, and I wondered if the pills might be to blame. They weren't helping much anyway, so I quit taking them. The blister went away. I mentioned it the next time I saw the doctor, but he said it must have been a coincidence.

Not long after, the drug, Bextra, was taken off the market in the United States. It had been linked to heart attacks and also to a dangerous condition called Stevens-Johnson syndrome — which can cause mouth blisters, among other things. There's no way to know if Bextra caused my problem, but it seemed like a reasonable idea, and I never understood why my doctor was so quick to dismiss it.

The episode came to mind when I read an article in the March 11 New England Journal of Medicine by Dr. Ethan Basch (<http://content.nejm.org/cgi/content/full/362/10/865>), an oncologist who treats men with prostate cancer and does research at Memorial Sloan-Kettering Cancer Center in New York. He argues that doctors, researchers, drug makers and regulators should pay more attention to patients' firsthand reports of their symptoms while they take medicines, because their information could help to guide treatment and research, and uncover safety problems.

Direct reports from patients are rarely used during drug approval or in clinical trials, Dr. Basch says. If patients' comments are sought at all, they are usually filtered through doctors and nurses, who write their own impressions of what the patients are feeling.

In addition, he writes, doctors and nurses "systematically downgrade the severity of patients' symptoms" and sometimes miss side effects altogether. One result is "preventable adverse events" — for instance, suicidal thoughts in young people taking antidepressants, or severe constipation in people taking a drug for irritable bowel syndrome, both of which might have been detected earlier if symptoms had been systematically tracked.

Dr. Basch, 42, said he first became interested in this subject around 2003, when he attended a presentation of the results from a study of a new cancer drug. The researchers had not found fatigue to be much of a problem, but other doctors in the audience said their patients had suffered terribly from it while on the drug, so much that some had to quit taking it. Somehow, the study had completely missed that finding.

Intrigued, Dr. Basch began to study people receiving chemotherapy, and to compare symptom reports by patients with those from doctors and nurses. The differences were striking. For every problem—fatigue, nausea, appetite loss, vomiting, diarrhea, constipation — patients reported it earlier and more often than did doctors and nurses.

Why does this happen so often? There's no simple answer. "There is a sensibility among some old-school clinicians that they have a better sense of their patients' experience than patients do themselves," Dr. Basch said. "But doctors and nurses bring their own biases to the evaluation. They might say, 'Mrs. Smith always exaggerates her fatigue—she says 9, but I rate it a 6.'" Three clinicians asked to rate the same patient's nausea will often give three different scores, he said.

The tendency to downgrade symptoms may be based on the doctor's knowledge that a patient is in the early stages of an illness and could be much worse. Or the doctor may be making mental comparisons with other patients who are sicker: "You think your nausea is bad, you should have seen the patient I saw this morning, let me tell you," as Dr. Basch put it. Sometimes, he said, the downgrading may reflect wishful thinking by doctors, who may think that a certain drug will help patients and don't want to take them off it.

Another reason, Dr. Basch said, is that "we live in a litigious society." Describing a problem in a chart creates a record that the doctor may have to act on. "There may be a defensive lack of documentation," he said. But he went on, "Increasingly, scientifically, we believe that whatever Mrs. Smith says is what Mrs. Smith is experiencing, and it's important to know how patients themselves feel about how they're doing."

But the doctor's perspective is important, too, he said, and he suggested that symptoms be rated the way the Web site Metacritic (<http://www.metacritic.com/>) rates movies: it posts two types of score, one from the public and one from professional critics. "I want both," Dr. Basch said. Sometimes the information is lost altogether, when doctors and patients, distracted by test results and treatment plans, forget to discuss symptoms. "This is where a checklist could help," he said.

Mistakes and distortions in reporting symptoms can be compounded in studies, where one researcher collects the information, another retrieves it from the chart and enters it

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into the study record, and still others evaluate it. The results can be like playing telephone. “There are multiple steps of transcription and information filtering,” Dr. Basch said. “We know there are omissions and misinterpretations at every step of data transmission. We know information gets lost.”

Patients may also tell doctors one thing and then write another in their own reports, Dr. Basch said; most say their written accounts are closer to reality. The idea of not telling doctors the whole truth struck a guilty chord with me. Growing up, I got weekly hay fever shots that I don’t think helped me at all. But I kept hoping they would, and the doctor was very kind, so whenever he asked if I was feeling better, I said yes, even though I actually spent most of August and September sneezing my brains out. This charade went on for years. Would I have been more honest in a diary? Maybe.

The Food and Drug Administration does have a system, Medwatch (<http://www.fda.gov/safety/MedWatch/default.htm>), that lets doctors and patients report problems that they think are adverse events from drugs already on the market. But it’s a passive system that waits for reports instead of actively surveying patients. Many people don’t know about it, and it has failed to catch some important adverse events, Dr. Basch said.

A better approach, he says, would be to have large numbers of patients filling out questionnaires before and after drugs are marketed. In an e-mail message, he said, “For example, in the postmarket setting we could ask 5,000 selected patients starting Bextra to report monthly (you would have reported the mouth sore without knowing if relevant or not, and this would then be pieced together with other reports).” If patients had been asked to report their symptoms while the drug was still being tested, he added, problems might have been detected before it was even approved.

Gathering the patients’ information would cost money, but not much compared with the overall cost of drug development and clinical trials, Dr. Basch said, adding that it would also save money by heading off potentially expensive problems. Dr. Basch said he was surprised to find drug companies enthusiastic about his research. “You’d think it would not be appealing to them, because you’re generating more adverse events,” he said. “But the grade of the data is superior. You catch a lot of baseline symptoms before people start the drug, so you can understand what’s probably related to the drug versus what’s related to the patient’s arthritis or whatever they had before the trial.”

Although the regular reporting may sound like a nuisance for patients, researchers find that many people are eager to have their say. In one study, Dr. Basch said, subjects “typed volumes” into a small online text box, even though they couldn’t see what they were typing after the first few sentences. “We’d get two pages of stream of consciousness,” Dr. Basch said. “The clinicians became overwhelmed.” The challenge is to create surveys that focus on what’s relevant — and yet still provide a way to describe symptoms the researchers hadn’t

anticipated. Dr. Basch is working on it, for the National Cancer Institute. “Patients have a lot to say,” Dr. Basch said. “We’re just waiting for someone to listen.”

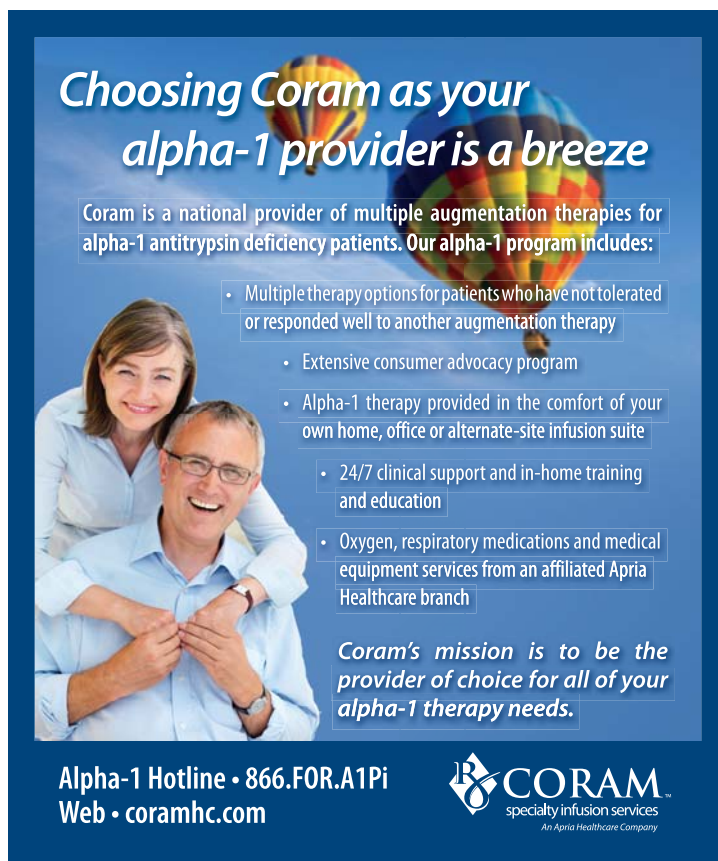
## Kamada Product Named Glassia

The U.S. Food and Drug Administration (FDA) has awarded the commercial name “Glassia” for Kamada Inc.’s intravenous AAT (Alpha-1 Antitrypsin) drug for congenital respiratory diseases. The approval is a necessary step for obtaining marketing approval of the drug in the United States. The Israeli pharmaceutical company said in early May it expects to receive FDA approval for its treatment of Alpha-1 Antitrypsin deficiency (AATD) in early July. Kamada said it has set up a U.S. subsidiary called Kamada Inc. as part of its preparations to market the drug in the United States.

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Just like in every organization, our funds are not unlimited. The 1AAT Grants may be suspended temporarily as we wait for additional grants and donations. If you would like to assist other Alphas through a donation, you may mail them to A1AA, PO Box 202 Wolfstown, VA 22748.

## Patients Should Do Research before Deciding Where to Get Their Transplants, Study Suggests

ROCHESTER, Minn.—BUSINESS WIRE

For patients in need of a liver transplant, their choice of a transplant center can make a noteworthy difference in their outcomes, according to a Mayo Clinic study presented at the American Transplant Congress under way May 1–5 in San Diego.

“We did find significant variation between centers in patient outcomes in the first year after transplant,” says Ray Kim, M.D., one of the lead investigators on the study. Previous studies have looked at outcomes based on factors about the recipients and donors involved, but no known previous study has focused on what effect the transplant center could have on patient outcomes.

Researchers documented an average 30 percent difference in risk for failed transplant between centers. Between centers with the best and worst outcomes, there may be as much as a fourfold difference in risk. Failed transplant was defined as either patient death or the need for a subsequent liver transplant within a year. “Though one intuitively expects a certain amount of difference between centers, this effect seems larger than previously thought. The bottom line for patients: do your homework before selecting a transplant center,” he says. But transplant center size alone, measured in patient volume, didn’t account for the difference in outcomes. “Results showed that the number of transplants performed didn’t materially affect outcomes,” says Dr. Kim. “This implies the largest center won’t necessarily have the best results. Similarly, a smaller center may deliver similar outcomes.”

Using data from the Organ Procurement and Transplantation Network, Mayo Clinic researchers reviewed data from 12,233 patients who received liver transplants to treat chronic liver disease. The data included transplants performed at more than 100 U.S. hospitals that did at least one liver

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The most common adverse events observed related to ARALAST NP included: headache (4 of 61 (7%) events) and maculopapular dermatitis (4 of 61 (7%) events).

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transplantation surgery from 2005 to 2008. Of those transplants, 15 percent failed within a year. The outcome differences between transplant centers were greatest during the first three months post-transplant.

Data used in the study was combined and analyzed without naming the transplant centers. “The goal of the research is not to point fingers,” says Dr. Kim. “The study was undertaken with the hope of finding ways for the transplant community to make the best use of a very limited resource, namely the donated organs. The data clearly showed that where the transplantation is done makes a difference whether the outcome of a transplant will be successful.” In the United States, nearly 16,000 people are waiting for liver transplants.

Dr. Kim notes that there may be several ways transplant center factors can affect transplant outcomes. The most immediate factor is quality of care provided at the center, including surgical, medical and nursing expertise. In addition, how patients and donor organs are selected for transplantation also contributes to the outcome. And last, where the center is located geographically has a substantial impact on availability and quality of donated organs.

Patients who need information about any type of solid organ transplant can find outcomes and statistics by individual transplant centers at the Scientific Registry of Transplant Recipients ([www.ustransplant.org](http://www.ustransplant.org)). The SRTR is administered by the Arbor Research Collaborative for Health with the University of Michigan, with oversight and funding from the Health Resources and Services Administration. Data are adjusted for organ health and the health status of the recipient

to provide an objective comparison of outcomes. Read more at <http://www.fiercehealthcare.com/press-releases/study-shows-liver-transplant-center-impacts-patient-outcomes#ixzz0nISqxUdp>.

*VIDEO ALERT: Additional audio and video resources, including excerpts from an interview with Dr. Ray Kim, are available on the News Blog. These materials also are subject to embargo, but may be accessed in advance by journalists for incorporation into stories. The password for this post is: kimtpx1.*

## Rapamycin Reduces Intrahepatic A-1-a Mutant Z Protein Polymers and Liver Injury in Mouse Model

Shalesh Kaushal and Mani Annamali, Department of Ophthalmology, University of Massachusetts, Worcester, MA; Keith Blomenkamp and Donna Halloran, Departments of Pediatrics, and Biochemistry and Molecular Biology, Saint Louis University School of Medicine, Cardinal Glennon Children's Medical Center; David Rudnick, Department of Pediatrics, Washington University School of Medicine, St. Louis Children's Hospital; Elizabeth M. Brunt, The Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO; and Jeffrey H. Teckman, Departments of Pediatrics, and Biochemistry and Molecular Biology, Saint Louis University School of Medicine, Cardinal Glennon Children's Medical Center and Department of Pediatrics, Washington University School of Medicine, St. Louis Children's Hospital; Exp. Biol. Med. 2010; 235:700-709, © 2010 Society for Experimental Biology and Medicine,

Alpha-1-antitrypsin (a1AT) deficiency is caused by homozygosity for the a1AT mutant Z gene and occurs in one in 2000 Americans. The Z mutation confers an abnormal conformation on the a1AT mutant Z protein, resulting in accumulation within the endoplasmic reticulum of hepatocytes and chronic liver injury. Autophagy is one of several proteolytic mechanisms activated to cope with this hepatocellular protein burden, and is likely important in disposal of the unique polymerized conformation of the a1AT mutant Z protein, which is thought to be especially injurious to the cell. Recent data indicate that rapamycin may more efficiently upregulate autophagy when given in weekly dose pulses, as compared with a daily regimen. Therefore, we evaluated the effect of rapamycin on PiZ mice, a well-characterized model which recapitulates human a1AT liver disease. Daily dosing had no effect on autophagy, on accumulation of a1AT mutant Z protein or on liver injury. Weekly dosing of rapamycin did increase autophagic activity, as shown by increased numbers of autophagic vacuoles. This was associated with reduction in the intrahepatic accumulation of a1AT mutant Z protein in the polymerized conformation. Markers of hepatocellular injury, including cleavage of caspase 12 and hepatic fibrosis, were also decreased. In conclusion, this is the first report of a

successful in vivo method for reduction of intrahepatic a1AT mutant Z polymerized protein. Application of this finding may be therapeutic in patients with a1AT deficiency by reducing the intracellular burden of the polymerized, mutant Z protein and by reducing the progression of liver injury.



## William H. Poppett Memorial Scholarship

The Alpha-1 Advocacy Alliance is offering the William H. Poppett Memorial Scholarship for secondary educations (college or graduate studies) to Alphas and children of Alphas who fulfill the requirements of the grant. The number of grants will be based on the donations received. The following rules apply:

- The individual applying for the grant must be at least a carrier of the Alpha-1 gene, the adopted child of an Alpha-1 individual or a first-degree relative of an Alpha-1 individual.
- The individual will submit an essay to the A1AA by a Word Document or by USPS mail by June 15 of the reward year.
- The essay should be a minimum of 750 words and a maximum of 1500.
- The composition must be the work of the individual applying for the award.
- Accompanying the essay should be a cover sheet listing the name, address, telephone, and email address of the applicant and the name and address of the school they will be attending.
- The decision of the A1AA will be final and announced publicly in *The Register* newsletter in the August issue.

The topic of the essay is as follows: How Alpha-1 Changed My Life.

If you have any questions, please call 866-367-2122. Email any question or submit your essay electronically to [scholarship@alpha1advocacy.org](mailto:scholarship@alpha1advocacy.org). You may mail it to Alpha-1 Advocacy Alliance, PO Box 202, Wolfstown, VA 22748.

	<b>Organ/Tissue Donor Card</b>	
I wish to donate my organs and tissues. I wish to give:		
<input type="checkbox"/> any needed organs and tissues	<input type="checkbox"/> only the following organs and tissues:	
Donor Signature _____	Date _____	
Witness _____	_____	
Witness _____	_____	



Alpha-1 Advocacy Alliance  
PO Box 202  
Wolftown, VA 22748

Address Service Requested

FOR INFO CALL: 540-948-6777  
Toll Free: 1-866-FOR-A1AA  
Fax #: 540-948-6763  
<http://www.alpha1advocacy.org>

## Inside: In Reporting Symptoms, Don't Patients Know Best?

THE ALPHA-1 FAMILY PROVIDING INFORMATION AND EDUCATION TO THE COMMUNITY.

## Alphapotamus: Are You Affected by P.P.H.C.R.?

I bet you don't know what PPHCR stands for, do you? That's because Alphapotamus made it up to represent some of the reasons why some of us start smoking or drinking when we know we shouldn't.

Before I tell you what PPHCR stands for, let's discuss why any Alphapotamus should not smoke or drink. Because we have the lovely Alpha-1 deficient genes floating around in our DNA, we have less protection for our lungs and liver. If we smoke, we will damage our lungs. When we smoke with the deficient genes, we will get sicker lungs younger than others. Alcohol is broken down in the liver and if your liver has any damage, any alcohol is not a good thing for your liver. Some doctors say moderate use of alcohol is okay IF you do not have any liver damage. How do we know if we have liver damage? Tests and scans and a doctor's close examination are the only way to determine that there is no liver damage.

So what is PPHCR?

**P.P. is Peer Pressure.** Do you try one cigarette because your friends are doing it or drink one beer because the adults are not around? Think before you make a decision like this without thinking it through. If it feels wrong, it usually is wrong.

**H. is Habit.** Did you start smoking or drinking because of wanting to fit in and now you are smoking all the time or drinking whenever there is beer or alcohol around? Do you find it hard to quit? Is it difficult to say no? This can be a habit or an addiction. You can be helped by reaching out to your counselor, doctor or parents to help. You are not alone and there is help.

**C. is Curiosity.** Many people start drinking and smoking out of simple curiosity and then get hooked by the habit or peer pressure. There is nothing wrong with trying new things, but make them healthy or nutritious or smart choices that will not damage your health.

**R. is Responsibility.** Taking personal responsibility for your own actions is the smartest thing you can do for yourself. Accept blame for poor choices and right the wrongs. You will some day be taking care of yourself and the decisions you make now, will affect how much you pay out for health care in the future. How much you spend on cigarettes and alcohol could buy a car some day, and it will determine how you will be able to live your life—actively or passively.

