My Journey with Familial Amyloidosis (TTR-FAP)

By Barry E. Breen

I am Barry Breen. I was diagnosed with Familial Amyloidosis in Sept 2009, Thr-Alanine-60 variant. This is my story.

Dedication

This story is dedicated to my late sister, Karen, who died in Oregon of "unknown malabsorption" at the age of 65 in 2007. Karen never knew her illness; the doctors could not find "anything" but never tested for amyloidosis, probably never thought of it. Her battle, although unsuccessful, inspired me to persist. Karen, I did! Your death and my battle may assist others in quicker diagnosis.

Karen Louise Jones, 1943 - 2007

My Journey with Familial Amyloidosis (ATTR)

By Barry E. Breen

This journey probably started long before I knew it began. Perhaps five or ten years before I noticed more serious, but progressing, health issues. I am a data nut, but I guess when you are an engineer by profession you have an excuse, flimsy as it may be. Since I had been getting annual physicals for most of my adult life, I had lots of data……all those blood chemistry tests. What is an engineer to do? Obviously, keep them in your computer along with all your medical diagnostic data! Yes, a nut.

One day in March 2009 a cleaning lady (who is a primary key player in this saga) was at my house. I hadn't been feeling all that good and we were talking about health matters when Helen said to me, "a friend of mine got seriously ill and his protein level was really low." Not one to let moss grow under my toes, off I went to my computer to look at protein levels in my blood chemistry. To my amazement my blood protein which had been constant at about 6.8-7.1 for a decade and a half suddenly dropped to 6.0 over a nine month period and was now somewhat stable at that value. When I reported this to physicians, I was advised that they really look at the ratio of the protein level to some other quantity. But, this has always nagged at me because "why would my protein level be stable for years and then suddenly change for no apparent reason?"

I went in an weighed myself and found I had lost a good 15 pounds (from a normal 155 most of my adult life to about 140). Coupled with the blood chemistry change, I started being somewhat concerned as I had had ever increasing bouts of irritable bowel syndrome (or that's what I called it—alternating diarrhea and normal movements, but more and more frequent diarrhea). Throughout the time leading up to all this in late Fall 2008, because of the alternating IBS like symptoms, I had seen a GI specialist who had previously performed routine colonoscopies and a prior endoscopy. He obviously checked for C-DIF and all the normal kinds of causes and could not find anything abnormal, and I did not respond to any particular medication to correct the IBS.

As the symptoms got worse and I continued to lose weight in late April, I was at my wits end, and my GI doctor put me in the hospital for a few days for observation and more tests. These included another colonoscopy and endoscopy with biopsies to check for any malignancies or other strange conditions, save one (*NOT amyloidosis at this time….who ever heard of that!*). There was an MRI of the abdomen looking for any tumors or other oddities, an MRA of the abdomen checking for blood flow, a Kidney-Urethra-Bladder (KUB) x-ray, an ultra-sound of the abdomen, and eventually a HIDA scan to verify gallbladder function. Nothing was found except the gallbladder had a really low "ejection fraction" of 6%. The gallbladder was removed within two weeks via cholecystectomy (laparoscopic procedure). I am certain at this point that my doctors thought I was, in fact, crazy or a hypochondriac—I'm not kidding.

One of the things I told my physicians is that my sister died of "unknown malabsorption" about two years previous at the age of about 65 (I was now 63). Many of her symptoms that were ongoing were things that I had just started experiencing. So, I was persistent and motivated to find out what could be wrong. I wanted to avoid the same situation if it was possible.

I had asked my GI specialist for a referral to a specialized clinic where I might seek additional medical evaluation, and I was referred to the Mayo Clinic in Jacksonville, Florida. I decided to keep my appointment at the Mayo Clinic even thought the gallbladder had recently been removed within the past month (only part of the problems or symptoms had resolved*)—I had the gut feel we had not gotten to the bottom of this*. At the clinic it was suggested I allow the recent surgery about 6 more weeks time to ascertain any other changes, perhaps for the better.

During this time I started noticing that I would get slightly light-headed or dizzy when standing up or sometimes when starting to walk from a resting situation; in fact I recall that happening for unknown reasons a month or two previous but ignored it at the time. I had a normal cardiology checkup scheduled for July and reported this to the cardiologist along with the history of my other symptoms. Although I wasn't due for a stress echo until the following year (had had one in 2007 that was normal), my cardiologist concurred that it would be prudent to do. Upon undergoing that test some real issues arose. My blood pressure was behaving abnormally (falling to really low levels) under stress and we actually had to discontinue the exercise portion of the stress test after about 7 minutes. I received a call from the cardiologist that night that he wanted to perform a catheratization (angiography) to look for any blockages. I asked him when he wanted to do it, figuring it would be scheduled next month; he said "how about the day after tomorrow?" I agreed and the procedure was performed. There were no blockages noted at all (I thought, hey, all that Lipitor over the years must have worked!).

When I went to the cardiologist for my "debriefing" (that's what we would call it in my flight test engineering profession), he said that he noticed a faint, but perceptible, difference in the ventricular wall thickness. It had increased by about 2mm from 2007 and seemed to show some sort of infiltration, a strange "glint." Coupled with my six month history of GI difficulty, he recommended I undergo a biopsy for something called amyloidosis.

At this time I had also recently established a new primary care (PC) physician. He was also consulted by the cardiologist and a "fat pad" and "rectal" biopsy were recommended and scheduled. As I had been through all this analysis and testing with no definitive diagnosis and, therefore, on no road to recovery, I had become quite depressed. My PC physician prescribed 10mg of Lexipro daily, and that helped a great deal with the mental anguish. Blood chemistry and urine tests showed no indications of, what they referred to as, "light chain" indicators for amyloidosis. I figured here we go with another test (the biopsies), and just knew they would be negative too—and I would never find out what, I now felt, was gradually sapping my life away.

What? What did you say?

POSITIVE?

I was sitting in the surgeons office to discuss the results of the biopsy, and he told me that both biopsies were positive for amyloidosis. That literally floored me. I had obviously looked up a little bit on amyloidosis since the biopsy and had found out that there is no medication which can cure it, that it occurs when your body produces an insoluble and "abnormally folded" protein. "Insoluble?" I knew what that term meant. One's body cannot rid itself of the substance (amyloid); it does not dissolve; therefore, wherever it goes it is likely to stay there. If it builds up in organs, it infiltrates the tissue and reduces or compromises the function of the organ until eventual organ failure.

At this point I went into high gear as far as where do I go, what do I do? Who treats or further diagnoses this strange sounding illness (why couldn't I get something I and others could at least pronounce?). I also set up an appointment with my primary care physician in five days. The initial biopsy result was provided to me on Sep 18, 2009 and that appointment was on the 23rd. I found there were three real centers of excellence regarding amyloidosis: Boston University, Mayo Clinic and Sloan Kettering. I am sure there are other fine institutions that deal in the illness, but these were the three top centers that my own research turned up. After consulting with my primary care physician, he recommended I return to the Mayo Clinic since I had established a prior relationship, and they were one of the "top three" on my list. That same day, I established an appointment for October 8 at the Jacksonville, FL campus.

As I continued my research in ensuing days prior to the appointment, I found there are two main types of "systematic" amyloidosis and other secondary types (secondary to other illnesses). The two predominant types are either AL (light chain amyloidosis, also referred to as primary amyloidosis) or ATTR (TTR-FAP amyloidosis or "transthyretin familial amyoid polyneuropathy"). ATTR is also referred to as hereditary amyloidosis. The secondary types are referred to as "AA". There are also some amyloidosis cases which are specific to certain organs (not systematic or system wide and not due to another underlying condition). It was at this time I recognized the seriousness of this illness. In AL the bone marrow produces the amyloid substance, and it is potentially treated by chemotherapy and a stem cell transplant to replace the bone marrow. In ATTR the liver produces the amyloid, and treatment includes a liver transplant. I am sure there are lots of valuable clinical trials and studies of various drugs to control or slow the amyloid production, but at this time, to my knowledge, no known, approved, medication cures the production (just the transplants mentioned previously). Further, ATTR amyloidosis is actually caused by any one of over a hundred known genetic mutations of the TTR gene, and this is why it is hereditary or referred to as "familial". If one parent has a specific TTR genetic mutation there is a 50% chance a child will have that mutation; however, it does not skip generations. So a child who does not inherit the mutation cannot pass it on.

By the time of my appointment at the Mayo Clinic, although a neophyte in medical things, I had a fundamental understanding regarding this seriousness disease and knew some kind

of unique challenge probably lie in front of me. It was at this time I was glad I had selected the Mayo Clinic in Jacksonville. Winter was fast approaching, and I sensed I might be spending some time in Jacksonville, Florida rather than Rochester, Minnesota. Being in Florida during winter rather than Minnesota seemed to have its perks. My appointments started and what seemed like "gallons" of blood for tests (and I hated getting blood drawn—even fainted at my military draft physical in 1970)—actually it was teaspoons, but it seemed like gallons! Then, there was the bone marrow aspiration. There is no way I can tell you this test doesn't produce some discomfort—it does cause some pain, but I had one of the best diagnostic technicians you could have. It is extremely short duration, but I think I want to be put "out" for this if ever repeated (but, I'm probably just a wuss). The wait for the analysis and results now began, and it can take up to 2-3 weeks for all the tests and analysis. I returned home to await the next steps.

It was at this time I recognized the importance of the initial timely diagnosis for amyloidosis by my cardiologist. His studies, his medical career, his attention to detail and commitment to patients culminated in a relatively early diagnosis for an illness that many times goes undiagnosed until it is too late (one is too weak for some treatments such as transplants). The illness is so rare (I understand~2000 cases in the U.S. identified a year out of 300,000,000 people) that it is frequently missed by physicians because the symptoms, taken singly or even together, can mimic other illnesses. Also, when tests come back negative, a physician not familiar with amyloidosis, might think a patient has a psychological disorder instead. The test for amyloidosis, the biopsies, are reasonably simple although performed surgically. Blood chemistry or urine tests cannot positively identify ATTR. Such tests can define the "light chain" (AL) variety through electrophoresis or immunofixation diagnostics of blood and/or urine. Diagnosis of ATTR requires ruling out AL and then confirming (determining) the DNA mutation of the TTR gene through mass spectrometry.

My return visit to the clinic in November provided my final diagnosis, ATTR amyloidosis. The genetic mutation, one of about 100 known to cause ATTR, was Thr-060-ala. Three days later I was in the liver transplant department at the Mayo Clinic in Jacksonville. My original intent if I had AL was to go to the City of Hope in Los Angeles, and if it was ATTR to go to Cedars Sinai in Los Angeles. The reason for those preliminary decisions were twofold: (1) I was born, raised, and spent most of my adult life in that area and had lots of friends for a support structure; and (2) Each of those facilities were in my health insurance plan for either a bone marrow transplant or liver transplant, respectively.

In the meeting with the liver transplant doctor, after his review of my condition and case, I let him know my leanings, and he offered me a data sheet regarding liver transplants. I think he knew *I liked data*……as I read through it, I found that one of the highest success rates for liver transplants in the U.S. was at the Mayo Clinic in Jacksonville, FL, and it had one of the shortest average wait times. I double checked the rates and wait times of the facilities which had been in my original plan; I immediately opted for the Mayo....*I could understand data*. I requested to proceed with the pre-transplant diagnostics to ascertain if I was a candidate for a liver transplant and if my health could sustain such a procedure.

Those appointments were scheduled for three weeks duration commencing December 2, and I returned home for Thanksgiving.

Looking back in retrospect, if I had had AL, my proper course would have been to head to the Mayo Clinic in Rochester, MN. In the months and years following all this, I learned the outstanding quality of the Mayo Clinic in MN and Boston University in MA for various types of Amyloidosis.

During the next few weeks I spent time doing even more research so that I would have the most complete understanding of where I was headed in this battle. I needed to ensure my health insurance rules were being followed for maximum coverage. I needed to arrange accommodations during my pre-transplant evaluation and post transplant recovery. And, I needed to arrange my immediate affairs to line up with a significant surgical procedure and an extended recovery away from my home. My goal was focused totally on my health; everything else was secondary—*clear my calendar*. I also had to let my close friends and family know the situation; I wanted to be totally open about it. There was no denial on my part. This had now become a "mission"–just like in my flight test engineering career, except my future life, or quality of life, depended on my success.

It was at this point, I passed the information to my one living younger sister (about 50 years old) and my deceased sister's children. After testing it turned out my younger sister had the same genetic ala-60 mutation. There was no doubt about the diagnosis at this point.

From reading medical papers I also was aware that the outcome, even with a liver transplant, was a statistics game. There was data to show that 50-70% of ATTR patients with liver transplants may continue progression of cardiomopathy symptoms due to wild type TTR protein or good TTR protein attaching itself to the previous mis-folded amyloid TTR substance. A fair number show some improvement in GI related issues. So, it was really unknown how my outcome might be, but other than medical drug trials this was really my only option for positive treatment. To me, if I was healthy enough for a liver transplant there was really no other choice

Well, I thought I had lots of blood drawn in November—*nothing compared to December,* but at least no more bone marrow aspirations. I do remember around 22 test tubes of blood drawn one or more times during the evaluation period. In addition to all the diagnostic matching and assessment studies, there were meetings with infectious disease doctors, pharmacologists, surgeons, nutritionists, financial advisors, and social workers. Some meetings required the patient *and caregiver*. A support structure was absolutely mandatory, and during the time waiting for this visit I was on the phone talking with long time friends in Florida where my employment had taken me 28 years previously. Little did I know that God's plan had arranged those assignments and travels to prepare for this current adventure. Additionally, my friends in Tennessee offered to assist in care giving. In all, seven good friends, my immediate and invaluable support structure, came to the Mayo Clinic and met with social worker and me. The social worker told me later that she had never had so many present for the support meeting. It was at this time I had a new appreciation for the true value of friends and friendships—*I was, indeed, a lucky person*.

December 24 provided me my best Christmas present. The transplant team and committee at the Mayo Clinic had completed their assessment, and I received a phone call that I had been approved for placement on the transplant list. My MELD (model end-stage liver disease) score, which determines one's place "in line" would be set to the default value for ATTR amyloidosis cases, 22. The reason for a default score is because the liver otherwise functions normally in such cases, but it is producing a substance which is causing other organs to gradually fail. Therefore, normal liver metabolic measurements cannot be used to determine the score. Some ATTR patients might have a higher score depending on whether other transplants are also required.

In order to be placed on the transplant list at a facility, in addition to the medical and health issues, one has to comply with the rules of that facility. Liver transplant success is enhanced by rigorous preparation & diagnostics and in hospital and post transplant procedures. The object is to minimize risk through rigorous processes. One of those rules for this facility was that an active transplant patient must reside within a four hour drive of the Mayo Clinic while active on the liver transplant list. Knowing this, I had arranged to temporarily relocate to Florida on January 6. My life was, quite literally, going to change forever on January 6, and I had no idea when, or if, I would see home again. I had little time to prepare, but my prior experience as a field engineer in relocating quickly and for various durations, sometimes lengthy, helped immensely. This plan of God must have included that prior experience and training. I knew what to take to live for however long it would be, days, months, or more than a year.

Again, my respect and gratitude for friends takes on new meaning. The son of some close friends who use to be my neighbor in California came to visit in Nashville after Christmas while on his winter college break. I knew Brandon since he was two years old, and he was currently running track and cross country at Iowa State as a post grad student there. He offered to drive with me to Florida. God must have arranged both our schedules to coincide on his winter break. We left for Florida with my essential belongings on January 5, as planned. On January 6 I checked in at the Mayo Clinic to start as an active candidate on the transplant list. My friends in Melbourne, Florida, who I met over 25 years before, offered me a place to stay while waiting. Again, I am forever grateful that this was in God's plan long ago. Who, in a million years, would have ever thought Barry Breen would

Rafting New Zealand 1994; Barry, left front, blue helmet

Wyoming 2008, R-Lazy-S

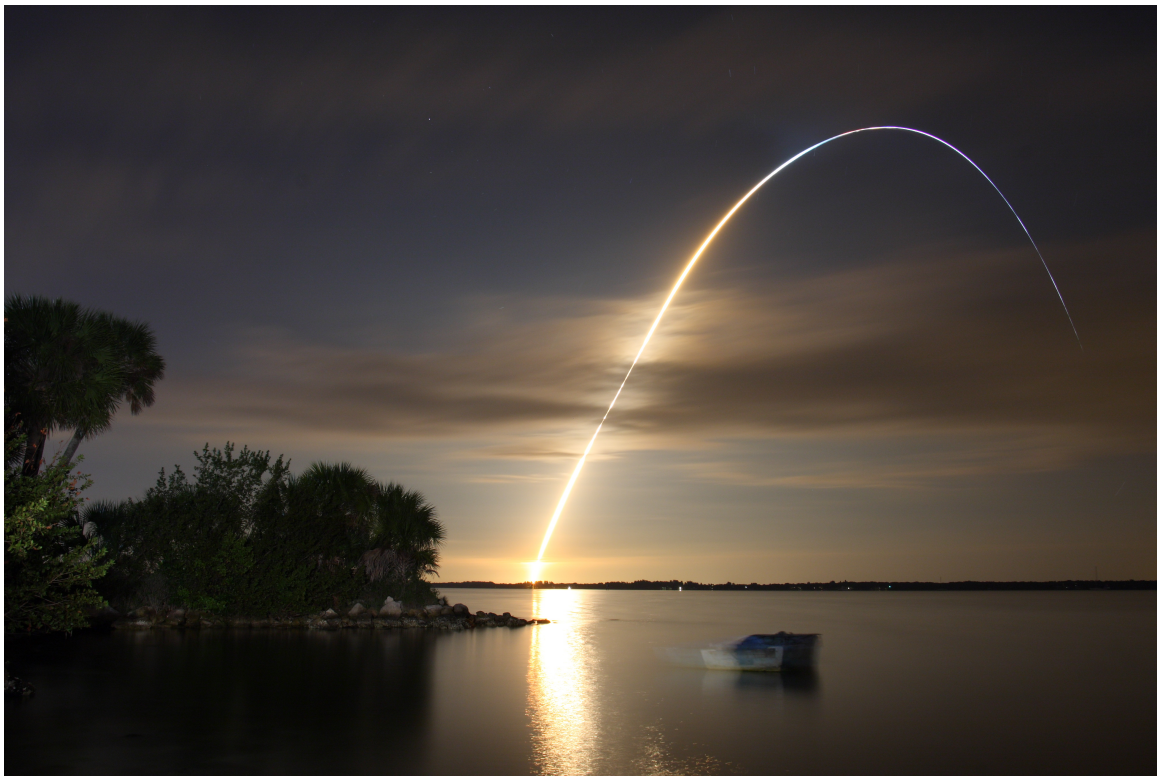
need a liver transplant? I had been so active and healthy. An active river rafter, I have probably over 15 rafting adventures and been down the Middle Fork of the Salmon River on 6 day adventures 5 or 6 times. An active horse rider, I had just concluded one of my many outings, this one a five day adventure Wyoming in Sep 2008, just before symptom onset. Active in caving, my most recent physical test was spelunking at Mammoth Caves, Kentucky for the Wild Cave excursion (5 miles, 6 hours underground, crawling and hiking through cracks, crevices, rocks and water) in Jan 2009, only 2 months before real systematic symptom onset—but, I do recall being exceedingly exhausted on that outing having done it five years before without such exhaustion. This list of activities for a healthy man go on and on, and now on the list for a liver transplant?

Wild Cave at Mammoth Caves, January 2009; L-R: Connor Stevenson, Lizzy Long, Barry Breen: 5 miles, 6 hours

As I settled in for the wait, I knew that my transplant doctor had advised the average wait could be 3 months for someone with my MELD score, but it was possible it might occur any time earlier, or later. The days started ticking off; I had to return to the clinic for follow-up blood work and health status every 6 weeks. I had two bags packed in my truck at all times. I tried to never be more than 15-30 minutes away from those bags. I had prepared a check list of what to do when I received "the call". My friends convinced me they should drive me, rather than me driving myself, when "the call" occurred. Being single I really had never relied on others like this before, but I agreed that that was the smartest decision (why would I drive 2-3 hours thinking about what lay ahead—*too risky for safety*). I now needed to adjust my lifestyle to count more on others.

Staying with an active family including a high school cheerleader and an eight year old football and basketball player made for a busy and activity filled period, one of my most

enjoyable life experiences. I had wanted to see a space shuttle launch since watching the very first shuttle launch, Columbia, in 1981—*yes, 28 years previous in Melbourne, Florida!* On April 5 I got that wish. My friends Red and Sherrie Jones, Ken and Cara Tracy and me all trekked up toward the Space Center for the view. Even though it was delayed for a day or so, we had a great time. And, there was the bluegrass festival in Polatka, Florida—with Red's barbeque and cooking to rival Emeril (Did you know Red is the best Barbequer east of Guam? Well, I think so!). I should not leave out all those basketball games at the high school and Nolan Tracy's flag football season—good job Nolan. Finally, I learned to love hot tea; Natalie Tracy made the best tea!



Launch of Space Shuttle STS-130 on April 5, 2010 at Kennedy Space Center, Florida

"The call!" It came at 1:28am on March 2—54 days after being activated on the transplant list. The voice on the other end asked if I could be at the clinic at 5:00am. Of course!! All that pre-planning would now pay off……*right!* What to do first? I remember standing up in a daze for a moment. Then within a minute I pulled the checklist out of my wallet and proceeded down the list. In a short while my friends were transporting me to the Mayo Clinic hospital. I made a few calls on my cell phone…..at 3am!

One of the most bizarre things which occurred is that I arrived at EXACTLY 5:00am, no earlier, no later. That accuracy and precision was to be the watchword of this mission. I was provided a "soft time" for surgery of 9am. The organ had not arrived yet, and so a final assessment by the transplant team had not been made, only the initial match and initial assessment. One thing about the Mayo Clinic is that unlike some facilities which utilize a procurement team external from the hospital, the Mayo uses their own surgeons and

personnel. This, I am certain, helps their success rate. I was prepped for surgery. I had been previously told as part of my training that 50% of the time a "dry run" might occur. This is when a decision is made upon organ arrival that the organ is not appropriate for the recipient. A second dry run can occur 30% of the time I am told. At 7:30am while I was taking a shower as part of preparation there was a knock on the door. A voice outside said, "Mr. Breen, it has been determined you have a hard surgery time for 10am". This meant the mission was a "go"; the count down had started; there was no turning back (the organ had arrived and been assessed as acceptable for me). It is difficult for me to put my feelings at that time into words. I had both a feeling of elation and sadness, sadness someone had given their life. All this preparation, and I was about to undertake the most challenging journey of my life. I guess you could say that so far, I had been in "Spring training".

10:00am arrived, and I was transported to surgery. As we went through the operating room doors it did look like a "Mission Control Center"! Except all those devices were going to be connected to me for life support and surgical support functions instead of to a flight test vehicle. You know, someone might think I would be worried, nervous, or have anxiety at this point. I must tell you I was totally at peace. I know that I had prepared as much as I could; there was nothing else I could do that I hadn't done, and the surgeons, doctors and transplant team had prepared as much as they could. It was in God's hands, and I was happy with that. No, I didn't have the slightest concern. I looked over by the wall on a table and there was a blue and white ice chest like you might see at a picnic. I knew that my new liver was there, *and this was no picnic*. Two surgeons were hovering over it. It was at this point that IVs were inserted in me, and it was "lights out".

They say I woke up in recovery, but I don't remember that. The time was about 4pm as I vaguely recall. I was in my room on the transplant floor. I was not in ICU. That is good news. Certain complications can result in one being taken to ICU first for stabilization before being taken to the transplant ward. I was transferred directly to the transplant ward. I was told that things went very well. They still needed to do an ultrasound the next morning to verify some things, but all in all things were VERY good. I really don't recall all that much pain. Sure, there was soreness as the incision point and I had various tubes in me, but I was in no particular discomfort that I can recall (sure, I'd rather be home watching a football game or playing the banjo, but for what I had gone through this was pretty darn good).

I was up and walking, with help, the next day. From the point you arrive in your room after surgery the goal is to get you ready for discharge. So, each day you do a little more so that you can be as independent as possible upon hospital discharge. I certainly wasn't running laps, far from it, but I thought walking around the floor, even slowly, was a great first step. One of the things that makes you minimize any anxiety is that you are well prepared for what you experience following transplant. This is part of the preparation/training which is included during the evaluation and assessment process for one's transplant candidacy. From the medication you take, to how often you take it, to your meals/diet, to what you feel and where you feel it, to taking your blood sugar measurement, this is all part of the preparation. In order for you to leave the hospital the

required medication (there is lots) must be also present BEFORE you can leave. So part of the arrangements are to ensure you have a pharmacy which can overnight the medication to the hospital and to you, wherever you are. The Mayo Clinic and their staff assist with this. Also, one must track their own blood pressure, temperature, weight, blood sugar, and medication every day after leaving the hospital and then continue with the ability to do that at home, as necessary. The clinic also assists you and your caregiver with training in this aspect.

After six days, with all my metabolism figures doing good things, I was released from the hospital to start my recovery in the next step toward independence. I had made arrangements for a hotel suite in a hotel that adjoins the facility (although there are many nearby). My caregiver and I moved into the hotel and were there for about 3 weeks. I underwent blood chemistry diagnostics at the lab at least twice a week. There were some ultrasounds and visits with various doctors. Primarily, they are keeping a close leash on you to monitor and adjust your immunosuppressant medication to get it just right. Mine was adjusted several times. The staples from the incision (all 55 of them) were removed 21 days after surgery (that process did not present any discomfort). I continued to make good progress and was released to come home about 4 weeks out from surgery.

At home now for about a month, no issues have arisen. Although I am not gaining a lot of weight; I gained a couple pounds and am quite stable in weight, albeit lighter than my regular adult weight, and at this point I didn't lose any from my pre-transplant weight. The Mayo Clinic provided me lab diagnostic orders for my home area, and I obtain blood chemistry each week on Mondays. Again, this is to keep track of the immunosuppressant levels for any necessary adjustments. My levels are very stabilized at this time. Within about two months (the four month period out from surgery), I will have ceased most of the immunosuppressant medication except for the life long Prograf (Tacrolimus). Also, when the four month point arrives I will visit the Mayo Clinic for a four month follow up where various diagnostics, including a liver biopsy will be performed. Unless there are adverse issues which arise, only annual visits are expected after this, around the anniversary date of the transplant each year. The regular blood chemistry frequency will gradually be reduced unless health issues are noticed.

There are various lifestyle changes which reduce risk of infection or illness. Obviously, when one is on immunosuppressant medication they are more susceptible to these things. But, there is common sense behavior to minimize risk. For example, it is recommended that transplant patients do not eat from public buffets such as a salad bar where anyone may have contaminated the food. Private gatherings are, of course, much less risky; one knows who is eating. Common sense really dictates behavior in this regard. Obviously if you're around illness or other infection, you are going to take precautions. Traveling in a crowded airplane I would most likely wear a surgical mask; the same is true for a crowded doctors office. I am sure there are other examples. For that reason I keep surgical masks on hand when traveling, and in my vehicle and my medication bag—just in case. There are other precautions and the Mayo Clinic runs you through an education module on that with the infectious disease folks. The biggest thing, and of course everyone should practice this anyway, is keeping your hands clean. For that reason I carry an alcohol based travel bottle

of hand sanitizer in my pocket most everywhere. When I leave a market or other establishments, I use it—*think of all those who has handled that paper money!!*

Those are the transplant related things that come to mind.

With regard to the familial amyloidosis (ATTR), I have accomplished much more research than before the transplant (and, I thought I had accomplished a lot at that time!). I have obtained numerous medical papers, and I subscribe to the amyloidosis support web sites and bulletin boards (here are a few):

http:// http://www.amyloidosissupport.com/support_groups/familial.html
http://listserv.acor.org/SCRIPTS/WA-ACOR.EXE?SUBED1=AMYLOID&A=1
http://health.groups.yahoo.com/group/AmyloidosisSupportGroups/

I am trying to locate others with the same genetic mutation as me (ala-60 or alanine-60) since symptoms, many times, are quite similar. And, in going back in time, I am trying to think of possible symptoms, that by themselves wouldn't tip you off you have amyloidosis (those that might have been real precursors to the onset of full blown symptoms which I described earlier in this discussion). I'll add to this paper as I ponder this over time.

As far as prognosis, that's really hard to say, but I am optimistic. Undiagnosed ATTR with ala-60 can have a pretty bleak outcome, although it can take 5-15 years for death as opposed to AL which, left untreated, can result in death within 1-2 years after symptom onset. Since I was reasonably healthy (that is, although I had diarrhea and light headedness for a short while, I had not had symptoms of heart failure) prior to transplant, I am hoping that slowing or stopping the progression may result in increased longevity and an ability to resume a more normal lifestyle. I am aware that there is data that further thickening of heart walls can occur (the process is not well understood). However, according to some data, the light headedness (orthostatic hypotension) and the digestion/GI issues, caused by a degradation of the autonomic nerves or intestinal damage, may resolve to some extent. Again this is a slow process as I understand it; so, time will tell.

Some day I hope to be able to write about my life "after" amyloidosis, and perhaps medical science and its researchers will enable me to do this with new discoveries in medicine. Just think if a medication could be produced which would enable the body to be able to get rid of the abnormal protein which has been produced, and prevent further amyloid production? There have been reports written regarding the diminishment of the existing amyloid substance, but I have not been able to find any specific therapy as yet.

The continued journey, post liver transplant—

Well, I just re-read what I wrote several years ago, and I have gleaned so much more, about the illness and about my personal battle, and it's time to write a follow-up.

I am grateful that my liver has performed so well up to this point. My blood chemistry is obtained monthly and the various counts that tell the organ's story are painting a good

picture. Very importantly, I take my immunosuppressant medication religiously. Most of the time my blood counts in this regard are smack dab on target, with minimum dosage (1 mg of Prograf twice daily with a count of 6-8). This is the only medication I take as far as the liver transplant goes. There have been no rejection episodes to date. I did develop some pleural effusion below my right lung at the time of the transplant, and that has stayed the same (not increased or decreased, but quite noticeable on an x-ray, but no resulting symptoms warranting addressing it yet).

Although disappointing, but fully known to me prior to the transplant for my specific mutation, the symptoms from the prior amyloidosis damage did not really improve, neither the gastric or the cardiac, but it is an interesting story. I had read enough papers to know that the body would not likely rid itself of the amyloid substance, and also that cardiac symptoms could continue to progress from either residual amyloid in the body or "wild type" TTR which could attach itself to the amyloid TTR already "seeded" into the heart tissue. And, in fact, my heart damage did continue to progress slightly. This manifested itself, eventually, in a complete cardiac electrical block (that is, when the atrium would beat, the ventricle did not know it, and it would fail to beat). Eventually, this electrical block was 100% (or "complete"); the symptom was that I experienced more and more light headedness to the point of fainting. One weekend about 9 months after the liver transplant, I could not get up without becoming light headed. I checked my pulse and it was only 36 beats per minute. That was a 9-1-1 call and a trip to the cardiac unit of the local hospital. They found the electrical block in the heart and installed a two lead pacemaker. When I woke up from surgery I felt like a new man. Since that time, another year and a half later to date, I have had very few light headed spells, although it is possible, but nothing like I was having prior to the pacemaker. I do remain with significant fatigue. My heart's ejection fraction remains at around 50%, sometimes a slight bit lower perhaps 45%.

To control the gastric distress (as in chronic diarrhea), I listened to the advice of some others and tried one semi-successful method, Tincture of Opium (0.6ml, up to 4 times a day and taken in about 2oz of water) and one Imodium tablet (2mg up to 4 times a day, taken with the tincture). There is a very fine line between diarrhea and constipation, and I now understand how the amyloidosis assists in causing the diarrhea). In my particular amyloidosis, my autonomic nerves were significantly compromised. These nerves control both blood pressure (when getting up or under stress) and digestive motility, regulating how fast food goes through the digestive tract. Many people are familiar with peripheral neuropathy afflicting hands, fingers, feet, legs, etc, and you directly realize that numbness has set in as the nerves don't conduct electrical impulses from the brain to those affected limbs, etc. In the same way, I suspect that the nerves to the intestines which sense the presence of food, etc., are interfered with, thus there is compromise control over the digestive process. In my case, there is resulting diarrhea and although there is not mal-absorption, I don't absorb the nutrients as well as I should. This also contributes to a slight anemic trend, depending on the amount of blood I have drawn at various times. Further discussion on this in a little while. The Tincture of Opium tends to slow down the motility in my gut which counters the effect of amyloidosis which is speeding it up.

Prior to my liver transplant I had no difficulties with my kidneys at all and my sugar level was perfectly normal. After the transplant my creatinine tended to rise as a result of the Prograf medication. The current levels of that medication causes my creatinine to be between 1.5 and 1.9, but my BUN to Creatinine ratio is fairly normal. The kidneys also produce a protein which is required for creation of red blood cells, and if their function lowers, sufficient quantities of this required protein might not be present. So this ties into the slight trend for occasional anemia, mentioned previously. To counter this, if my hemoglobin count gets below 10.0 (into the 9 range), I receive Procrit injections, as necessary. My blood sugar count remains completely normal.

The final symptom with which I have to combat is edema in my lower legs, ankles and feet. This has also remained the same, or about the same, since my liver transplant. Lasix would normally be something to take, but Lasix can adversely affect the kidneys over the long term, and I want to try and not stress the kidneys any more than absolutely necessary because of the Prograf. I try and keep my legs/feet elevated when seated, if convenient, and use calf length compression socks at times. With these actions, many times I have little to no edema in the morning when I awake.

So there you have my symptoms and how I deal with them. They are reasonably stable, as no more amyloid is being produced from the liver. But, the damage that causes all of these things remains, and appears, un-reparable at least over the last approximately three years since my transplant. And, as measured previously, the heart damage actually continued a slight progression over a 9 month period, but now appears stabilized.

Because it was known my only recourse was a liver transplant, and the Mayo at Jacksonville, FL had such a good track record in that regard, I immediately proceeded toward that end with them. However, other than the diagnostics for typing and treatment, I had no other detailed amyloidosis tests and evaluation. So, after I was stable and two years out from the transplant, I scheduled appointments at the Mayo campus in Rochester, MN. Specifically, because of the cardiac damage I wanted to determine whether a heart transplant was something that could further assist in my health struggle. I also wanted to learn anything else regarding my particular health status that could assist me in a better long term quality of life.

In Rochester I underwent tests to determine the overall affect the illness had on my autonomic system as well as direct GI involvement (stomach and intestines) and my cardiovascular system. In the end, it was determined that the heart was only about 25% of my issues, and the risks of further significant damage from a heart transplant would be much greater than any benefit to be gained by that action. The autonomic nerve and GI damage, prior to my transplant, were most of the problem now resulting in my current symptoms. The mitigation efforts previously described here are all that can really be done to improve quality of life. Beyond these, I must learn to live with my lot in life.

I and others with TTR-FAP are awaiting the development of two kinds of medication. The first is something to stop the production of amyloid by the liver, removing the necessity of a liver transplant. The second, for all amyloid patients, is a medication which will remove

the amyloid substance from the body and allow or enable the body to repair the damage done to the various body systems. Although there are reports and stories here and there about reduction in amyloid, after treatment, I currently have not experienced that. Currently (mid-2012), two medications are being developed to reduce production or stop production of amyloid (by liver). One is Diflunisal and one is Tafamidis. Tafamidis has not been approved in the U.S. but is approved in Europe and undergoing trials in the U.S. As yet no medication is on the horizon for the body to assimilate the amyloid substance, thereby getting rid of it and enabling organ repair.

For those reading this who have already been diagnosed with a TTR-FAP gene mutation from a parent, but have no symptoms, your question is: What do I do since I have no symptoms right now?

My advice is to get a complete cardiac exam no less than every two years, until age 50, and then every year (to include echocardiogram and ejection fraction (EF) determination under stress). Both blood pressure and EF can trend low if the heart is affected. Also, if neurologic function degrades (peripheral nerves—finger, hands, toes, feet legs) get heart checked as above and, also go to an amyloidosis center of excellence for nerve diagnostics. If any light-headedness starts occurring which has not occurred previously (dizzy, fainting, black out, etc), again go to a cardiologist and an amyloidosis center of excellence for diagnostics on autonomic nerves (orthostatic hypotension can cause low blood pressure because of dysfunctional autonomic nerves). As well, diarrhea increasing in frequency for no known reason (also can be a result of autonomic nerves).

The point is, get to an amyloidosis center of excellence if at all possible.

Why not your own doctor? That is fine to do in order to relate all the symptoms to him AND that you have a genetic defect (which you already know predisposes you). He/she may request a "fat pad" and "rectal biopsy" and certain blood and urine tests, but understand that ONLY a biopsy, performed correctly and read correctly, can confirm or rule out amyloidosis (but cannot type the amyloidosis). Facilities which have dealt with amyloidosis patients frequently are the best places for these things. Also, the facility (Center of Excellence) will want the actual biopsy tissue samples (not just the reports); they will examine the tissue again. I relate this to you as I would prefer to be a patient rather than a guinea pig, so to speak.

Amylodosis is an unforgiving, deadly illness if left untreated or diagnosed too late. And even when treated it may merely extend life more than those untreated. *The early diagnosis and start of treatment are absolutely critical in the scheme of things,* but there is no treatment without symptoms. Therefore, if one knows they have a gene mutation which causes amyloidosis, they should be on the lookout for symptoms, but NOT paranoid---hard to do, I agree. I assure you "time is of the essence."

Because so few doctors have ever treated an amyloidosis patient (perhaps only one or two in their entire career), they are not normally prepared to go down that road. Amyloidosis symptoms mimic many, many normal, curable illnesses (the kind physicians see all the

time). So physicians head down those roads; the ones most traveled. Specialists do the same thing. Then they reach a dead end. At that point a year or more in wasted time may have occurred (sometimes yearS). That year or more in time lost, could well cost one their life. The illness works its misery quickly. One must be aggressive and pro-active in their relationship with physicians in dealing with diagnosis, treatment and monitoring. I use to call it being your "medical program manager." You will not likely find a local "amyloidosis doctor" so for the most part stop looking there. This illness requires a TEAM of specialists in the fields of cardiology, gastroenterology, neurology, nephrology, and hematology and a specialist to coordinate the required actions. All of those systems can be affected, and usually there are multiple systems (as in two or three) involved. You can see why doctors get led down stray paths to dead ends. Centers of excellence put teams of specialists together who typically see amyloidosis patients. That way they can compare notes. In many cases amyloidosis patients do not respond to treatments the way "normal" patients would. So, there is no time lost on the learning curve or lessons learned. That's why a center of excellence is a wise choice.

An amyloidosis patient must be a pro-active patient. They will want to know the name of THE physician at the Center of Excellence who is their "go to" person for coordinating their amyloidosis treatment. One MUST identify this person. Another responsibility is becoming educated, much more than "normal" patients (it takes time, but more and more knowledge will gradually sink in, repetition is good). I consider maintaining copies of all my records my responsibility (I scan all lab reports and all reports of procedures/results and consults). Usually I just go to the facility web site and download them. I also have a scanner at home for those which might need to be scanned. Another facet which I consider my responsibility is to keep copies of my blood chemistry reports and understanding what things are pertinent to me, and how to understand them. I request the physician ordering the test to instruct the lab to FAX or mail me a copy. Again, this is education and it takes time.

Well, I hope to be able to write a few additional notes at 5 years, 10 years, 15 years out…… Time will tell. In the mean time I will learn to live with my TTR-FAP damage while watching the horizon.