

# Amyloidosis Support Groups

[www.AmyloidosisSupport.org](http://www.AmyloidosisSupport.org) Toll Free 866-404-7539

## ATTR 2015- Q & A

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### Q&A:

**Q: Do providers recognize amyloid more now, with the increased scientific activity around it?**

A: No. Even people with relatives who have had amyloid often go for a long time with symptoms but not diagnoses, including much mis-diagnosis.

**Q: If we have the gene, should we opt for biopsies that are more sensitive than fat?**

A: Dr. Benson waits until there is a therapeutic intervention. If some preventive treatment developed, then detecting earlier will be important. GI biopsies are becoming better tolerated, so may be an option to consider. Heart biopsy is riskier, so not a ready alternative to fat biopsy. Note: You can ask that old biopsies be tested with Congo red for amyloid.

**Q: Are there simple instructions about how to get genetic testing?**

A: Talk to a genetic counselor who is familiar with amyloid. Check out Alnylam Assist.

### Is Amyloid more known among ophthalmologists than among others, such as cardiologists?

Probably. Most ophthalmologists probably recognize amyloidosis in the eye.

### Are macular degeneration and wild type linked (cardio)?

We have no indication of this

### Why doesn't exercise strengthen my legs?

You may not notice benefit, but it is probably still of value. If you don't exercise, your capacity may decrease, so even staying the same may be a good thing. If your heart and nerves work poorly, you can compensate by keeping the rest of your body in good shape.

### Termination of open label?

There is no indication of terminations of any of the open label studies.

### Can you have different types of amyloid?

It is possible, but would be very rare. The pathologist has never seen two types in a mass spectrometer.

### Show of hands, significant eye involvement?

4 out of about 150 audience members raised their hands.

### Is research being done for medications to penetrate the blood brain barrier (which keeps some medications in the body from reaching the eye and brain)?

We know of none, but ophthalmologists inject all kinds of things into the eye – ways may be developed to get around the barrier.

Cardiologist amyloid specialists discussed Diflunisal yesterday, and have many reservations (ask Martha Grogan). There are no medications that have been shown to improve the amyloid heart.

### **Are wild-type studies planned?**

A Pfizer trial (closed to enrollment) includes 70% wild-type. (About 10 months into a 30 month trail). Another study is enrolling wild-type?

What is meant by “limit your alcohol intake”?

Usually, one unit (one beer, one shot, one glass of wine) [per day, I assume]. In small amounts, the cardiologist are not very restrictive in amyloid pts. Folks on a transplant list are expected not to have used alcohol in the past 6 months before transplant.

### **Any known trigger for genetic expression? Why does age at onset vary within families?**

We don't know.

### **Amyloidosis is not known by MDs in my community. How do I change that?**

MDs don't like to miss things. So send those who missed the diagnosis (in a non-litigious way) a note when you find out what you have, to let them know and educate them. At Cardiology meetings, there are sessions on amyloidosis, and they are usually very well attended. NIH has a request for funding applications for systemic amyloidosis (RFA, not RFP – i.e., there are no dedicated funds, and the reviewing committee is often uninterested). PYP is easy, and is going to “blow ATTR detection by cardiologists out of the water” – i.e., increase it a lot. Get your local hospital to give a grand rounds – Muriel can help arrange to get one of our experts to give that; there will be a small fee, but the hospital often covers that.

### **I'm an asymptomatic gene carrier. I have a biopsy showing amyloid. (i.e., positive with Congo red) Do I need to get it typed?**

No, except to rule out other reasons that a Congo red could be positive.

### **Can dysplasia [in the absence of atrial fibrillation] lead to stroke?**

No. ... But it can be very important to be on anticoagulants. Use of anticoagulants for folks without atrial fibrillation depends on other factors. Have a discussion with a cardiologist who understands amyloid. It is important to recognize how common atrial fibrillation is in ATTRwt.

### **Is the amyloid-related stroke location specific to any one area of the brain?**

No. But the risk of subdural [bleeding complications?] is about 3 times that of normal.

### **How often should PYP or ECHO be done to look for advancement of disease?**

No one knows. There are no standards. In ATTRwt, disease advancement is slow. Ejection fraction interpretation varies from provider to provider, by as much as 10%. PYP scans have not been shown to find amyloid well, but may discriminate between AL vs. TTR. It is a simple test, with radiation exposure equal to about a breast exam. It is easy to read, and is highly indicative of TTR amyloid. It is being studied as an early indicator of amyloid – it may detect it before cardio measures.

### **Can PYP replace cardiac biopsy for showing ATTR?**

Some of us hope so. Blood tests plus PYP may become the 1<sup>st</sup> screen. It may miss some small portion. PYP does not distinguish between wild-type and familial TTR. It does not seem to detect advancing disease among the very sick: PYP did not show difference over time in fairly sick patients who had advancing disease. The use of cardio biopsy is likely to decrease. Amyloid expert cardiologists are using it mainly to get folks into clinical trials, not of diagnosis.

### **Can we use PYP to detect ATTR earlier among carriers?**

Maybe – and some other tests are promising for early detection (Martha Grogan).

### **This community is a gold-mine for gene-positive, symptom-negative people. Can't we take advantage of this?**

Having a community-run registry could help a lot in assessing ways for early detection. Talk to Muriel if you are interested in creating such a registry.

PYP is done in Europe as a whole-body scan. In US, it is used by cardiologists, focused on the heart. An SAP can tell about amyloid in other organs, and not the heart.

### **When will the patient education booklets be available?**

In a few weeks. It covers familial, wild-type, and non-TTR amyloid. TAKE THESE BOOKLETS TO YOUR HEALTHCARE PROVIDERS.

### **What changes in the clinical trial neuropathy measurement scales are significant, and what do they equate to in real life?**

A challenge in clinical trials is to measure neuropathy in a way that can detect change. Neurologist panel decided that a 2 point change in the NIS scale was the minimum detectable by a neurologist. The Diflunisal trial found a 20 point change. This equates the going from getting out of a chair easily, to having trouble getting out of a chair.

### **Diflunisal – I've been on it for 25 years [I may have mis-heard that]]. I have been stable for 8 years, in symptoms. Why not use it?**

Many patients with heart failure have too many other things going on to make Diflunisal an easy choice. It is a risk-benefit decision, and merits thought and caution among patients with heart failure. Basically, we do not know the impact among amyloid cardiac patients, so it would be great to have more study of this. So we tend to be cautious, given the impact of Diflunisal in other types of cardiac patients.

### **Should asymptomatic carriers take Diflunisal?**

We are moving in that direction. We don't have a lot of evidence to guide us. We wouldn't recommend in it a 2-year-old with the gene – the kidneys don't like NSAIDS given chronically, and the protein does not start mis-folding until much later in life.

We don't know when to start screening (how long before onset occurred in the patients' relatives).

Some would start Diflunisal at 1<sup>st</sup> sign of symptoms, if they would tolerate it. Remember, not all carriers develop disease, so the Diflunisal may bring risk without benefit. Bottom line: When disease manifests, most see Diflunisal as being useful.

There is no clear consensus; talk to your provider, and make your own decision.

### **Can Diflunisal replace aspirin for preventing heart problems?**

No, they have different mechanisms.

### **What is informed consent for genetic counseling?**

Having a good understanding of the benefits and risks of having the test results (the information) and what you will do with that information. We do not recommend testing below age 18 for any adult-onset disease.

### **What testing would you do for someone who starts Diflunisal, and how often?**

Some panel cardiologists check every 3-4 months. Another cardiologist checks every 6 months.

### **If someone does not tolerate Diflunisal, should they try again after a break from it?**

No. Yes. Answers varied. Some intolerance may happen as you go onto it, as happens with many drugs, so don't necessarily give up early. (In Canada, Diflunisal is recently no longer available. But note that Canadians are not excluded from US clinical trials. Doctors in US or other countries may prescribe it for you.)

### **Is leptomenigial disease an FAP?**

Leptomeningial disease: 5 mutations can cause amyloid on the cover of the brain (on the brain side of the blood-brain barrier,) where there is limited exposure to drugs being tested for treating amyloid. In Japan, they are examining injecting some of the drugs into the eye (on the brain side of the blood-brain barrier). Getting drug to there is a hurdle we have yet to pass. It is not clear what measures the FDA might accept as evidence of efficacy of such treatments.

### **What medication should be used for anti-coagulation?**

We don't have information whether the new anti-coagulants are better than the old ones for amyloid. The decision is patient-specific. It may depend on side effect preferences and other drug-specific characteristics, cost, and the patient's disease characteristics.

### **Getting life-insurance after genetic testing:**

Life insurance companies sometimes have refused coverage of persons with family histories of ATTR, with negative test for the gene. Not all life insurance companies ask about the genetics. Consider getting life insurance before getting genetic testing. The question life insurance companies ask vary; some may ask a question that addresses the issue squarely, and some may not.

### **Are there NIS (neuropathy) scores needed to qualify to get into a clinical trial?**

Clinical trials are designed to include folks who will worsen if the medication is not given, or is not effective. Required NIS scores may be from 10-85, 5-130, 5-100, ... - usually that means more than just tingling as a symptom..

### **What type of eye problems occur?**

Problems are vitriol opacity (like "floaters").

### **What is relation between multiple myeloma & ATTR?**

There is no relationship. AL is related to multiple myeloma.

### **My kids (age 50) are afraid to get tested, for fear the information may be used against them regarding long term care insurance. What should they think about this?**

They should identify clearly what is keeping them from getting the test. Consider getting set up with insurance before testing. Even if they are not tested, LTCare insurance could deny coverage after it begins due to family history of amyloid. There is a 2 year contestability period. Be honest in answering the questions they ask. They may get your medical records, and refuse coverage retroactively (they would return your paid premiums).

## **Amyloid in the heart - take Diflunisal?**

**There is no medication yet proven effective for amyloid in the heart. Look to randomized clinical trials for evidence. Discuss with a provider who understands ATTR and your case, and make your decision.**

## **Are leg cramps common? What do people do about it?**

Maybe stretch before bed. Massage may help. Maybe drink quinine water (or tonic water) before bed. Some patients find yellow mustard (has turmeric) helps. Cramps may be aggravated by medications [diuretics?]. Exercise may cause or aggravate cramps, but don't avoid exercise. (The evidence seems to be from pts experiences of what works, not from studies.)

## **I thought insurance companies could not inquire about genetic test results.**

That covers health insurance and employment (by large employers – i.e., over 15 employees. Does not apply to US military, but not long term disability or life insurance.

## **Using Diflunisal after heart and liver transplant.**

Main issue may be renal function, and interaction with anti-rejection drugs. But Diflunisal has been prescribed by our amyloid expert cardiologists after transplants.

Social security disability:

ASG went to the social security admin. About the labeling on fast-track disability social security. If you have AL you are automatically fast-tracked. If you have ATTR and want to apply for fast-track social security, you are considered on case-by-case. Your doctor has to indicate that you are eligible for fast-track eligibility.

## **(Some question about a detached retina, Johns Hopkins providers)**

[I missed this.]

## **I was prescribed Florinef for an eye problem, and had a bad reaction. Should I keep trying?**

Florinef is a tough drug. You may or may not need it.

## **Will there be a published summary of the Paris meeting next week?**

Muriel expects to get results of the pharmaceutical company presentations. Muriel will share those. There may be an abstract book published, which Muriel would share.

## **Does the amyloid make you more tired? Does an increase in fatigue, and increased bowel problems, indicate advancing disease?**

Fatigue can be caused by many things: medication, disease progression, your physical conditioning. Bowel function can also be greatly affected by medications (as side-effects).

## **Antibodies to affect amyloid deposits**

A recently published study of SAP, a substance that tracks amyloid, indicated antibiotics might decrease SAP (and so, probably amyloid). The idea is that antibiotics may grab onto and dissolve amyloid. Evidence is not yet strong.

## **What is policy for travel expenses related to clinical trials?**

One trial has a maximum of \$3500 for travel during the trial. The amount can be site-specific, and varies by trial. Find out about it as you look at the consent material for the trial. One trial gives subjects a debit card on which they can charge expenses.

### **ECGC - what dose, what side-effects?**

The study used 500-700mg/day. Green tea extract may create aggregation of toxic form of amyloid [DR BERK – DID I GET THAT RIGHT?], as well as breaking up some amyloid aggregations. Clinical trial participants usually are not allowed to take ECGC. Are there long term effects of living with level of TTR? We don't know. It is being studied?

Can amyloid aggregate in odd places like joints, and cause pain and problems?

It has been shown sometimes to aggregate in muscles and tendons.

### **What is the best way to prevent weight loss and to rebuild weight?**

Pay attention to nutrition. Treat symptoms (nausea) and tings that may cause loss of appetite.

### **How to address obstruction in bowel wall that leads to weight loss?**

Weight loss is not necessarily due to amyloid in the bowel. It is often due to improper nerve signal to the bowel, causing diarrhea. Why don't we have gastroenterologist on the panel? Because the problem is neurological, not the gut itself. There may be amyloid there, but the neuropathy is the problem. Intestinal biopsies can be sent to a center of excellence for testing for amyloid.

I have a gastroenterologist who wants to do all kinds of gut studies, when I think ATTR is causing my problems. What do I do?

Some tests may be useful – ATTR may not be causing all the problems. But get them talking to an amyloid expert.

### **Will soaking in Epson salt help with leg swelling?**

It may help decrease cramps. It may not help swelling in the legs – that may or may not be due to fluid retention. Your diuretics may need adjustment, or you may need a different diuretic. Or the swelling may not have to do with fluid overload. Consider using stockings; put them on before getting out of bed. There are alternatives to prescription stockings – Ace bandages - but get something that is proven – talk to a knowledgeable doctor. Talcum powder can make putting on stockings easier.

### **Why is it important whether your mother or father passed the gene?**

A Japanese study found “anticipation” when the gene comes to the son from the mother: earlier onset, more severe.

### **GI symptoms are a huge part of the symptoms we experience. It is not all about motility. A GI specialist helped me (developing and maintaining a protein wall), and I have much better control now than I did.**

Muriel will look for someone to include. (Audience clapped at this). GI specialists are also expert in dealing with bacterial overgrowth. A lot is being learned about the microbiome of the gut right now, in medicine in general.

### **Tafamidis and Diflunisal – what are the differences between these stabilizers?**

Cost. Side-effects. Tafamidis may be a better stabilizer. Jeff Kelly helped establish both as treatments. Diflunisal has anti-inflammatory effects that may help with neuropathy, and has other potential effects (good or bad). Availability – tafamidis is not available in the US, while Diflunisal is. Much is yet to be learned about what the best dose [of tafamidis] may be.

### **What causes my excessive sweating?**

The autonomic system (neurologic) controls that, and many other things. Neuropathy from amyloid causes the problems.

### **Will a liver transplant improve autonomic system abnormalities?**

Yes, sometimes.

### **My relative with ATTR is very weak and thin. I worry he will hurt himself when he exercises. Should he exercise?**

Doing what you can to maintain muscle mass is important to quality of life, and may have other limited benefit. He should do what he can.

Constipation? Try mirilax twice per day, rather than once per day?

Will the drugs being tested ever be used in combination? Probably.

Effective stabilizers may decrease or halt progression, but may not reverse it. We are likely to use combinations to get the greatest effects. In HIV, combinations of medications have had very positive interactive impacts. That could happen with amyloid.

Ligaments may be directly affected, and stress on ligaments increases as muscle mass decreases.

### **EPO4[?] – may it be considered genetic?**

We've seen it in heart and kidney. [I MISSED THIS ANSWER FROM DR BERK]

### **Can I talk to someone to get into a trial?**

You have to be screened to get into a trial. Two major amyloid neuropathy trials (only one accepting wild type) may close enrollment by the end of the year, so if you want to get in, try now – screening often takes a month, so you have 2 weeks to get started to get in before they may close. See the ASG website for information about the trials.

### **If I like a doctor on the panel, how do I get my doctor to let me go to that doctor for a 2<sup>nd</sup> opinion?**

Any good doctor should support you seeing an expert. You are in charge of your care – you should insist in getting the care you believe you need. The panel doctors are very good at soothing the egos of other doctors.

### **[I think I got this question wrong] I want to switch clinical trials. How do I do this?**

[I MISSED THE ANSWER]

### **Are liver transplants a thing of the past?**

In Portugal, with tafamidis, the use of liver transplants had decreased, and people are more circumspect about getting one.

### **Should autonomic testing be routinely done at time of carpal-tunnel surgery (for everyone)?**

Maybe. Cleveland Clinic is doing a study of testing samples from carpal tunnel that has no obvious cause, and following those patients to see if they later develop ATTR.

Hand surgeons are high volume, and do not want to take the time to extract and save a tissue sample.

In families with ATTR, it should be done.

### **Should there be a national ATTR registry?**

Pfizer has the THAOS registry, which is useful but imperfect. The ASG has a wide reach, and could gather some very useful information.

### **Are there fibril-destroying drugs in trial?**

Yes, for AL. There is a drug aimed at “sucking out SAP” (part of the amyloid foundation), but it was not very effective. They are trying to go further, adding other medication to the process. It is a work in progress.

### **What are the main cardiac markers?**

BNP/ProBNP, & troponin