

New NP-C Clinical Trial Starts

September marked the start of a new clinical trial at the National Institutes of Health (NIH). A drug that is thought to fight oxidative stress in cells is being administered to a group of NP-C patients in the hope of slowing down the disease process.

This clinical trial was started at the NIH Clinical Center this past September by lead researcher Dr. Denny Porter. The goal is to test N-Acetyl Cysteine (NAC) in 30-35 NP-C patients over the next year. Although, Dr. Porter does not envision that NAC will stop the progression of NP-C, he is hopeful that it will address one aspect of NP-C and will be an important therapeutic player in NP-C treatment, when combined with other medications.

This clinical trial grew out of a Natural History study at the NIH, which has been supported by the APMRF, and has made great progress in understanding the NP-C disease process. Since starting the Natural History protocol in August of 2006, 45 patients with NP-C have been enrolled from the United States, as well as from the United Kingdom, Costa Rica, Dubai, and Lebanon.

The team of researchers at the NIH, working with Dr. Dan Ory (Washington University in St. Louis), identified a pair of oxysterols in the blood of NP-C patients that may form the basis of a diagnostic test and may provide an outcome measure for clinical trials. Oxysterols are produced from cholesterol in cells that are not able to normally metabolize oxygen. This latter problem is known as oxidative stress.

In addition to the oxysterols, these researchers found that a number of other laboratory tests indicate increased oxidative stress is present in NP-C patients. Oxidative stress damages proteins and lipids. Thus, this secondary damage compounds the problems that the cell has already incurred due to the cholesterol and lipid accumulation. In NP-C there is an accumulation of oxysterols because of the intersection of free cholesterol accumulation and increased oxidative stress. Dr. Porter notes that these oxysterols may be bioactive and thus toxic; however, at this point this is a hypothesis. The oxidative stress is potentially making sick neurons sicker. By correcting the oxidative stress he hopes to protect the neurons as much as possible. Hopefully, if some of the stress is eliminated, the cell can better deal with the primary insult.

Identification of oxysterols and evidence for increased oxidative stress in other blood tests in NP-C patients has led to the initiation of this therapeutic trial which will test the efficacy and safety of NAC to reduce oxidative stress in NP-C patients. NAC is a modified amino acid that is absorbed well by the body. In the body it is rapidly converted to the amino acid cysteine. Cysteine is then converted to a chemical called glutathione. Glutathione is a critical chemical that the cell uses to fight oxidative stress. Thus, NAC is a prodrug for glutathione. Glutathione itself does not get absorbed well or cross cell membranes. This led Dr. Porter to select NAC because it supplements the supply of glutathione in cells and directly addresses the issue of increased oxidative stress at a central and critical point. This would be in contrast to CoQ10 or Vitamin E that only addresses one aspect of oxidative stress. NAC has a very good safety profile and has been used in children for other purposes.



Nicole Yanjanin, CPNP and Dr. Denny Porter

This drug trial is focused on biomarkers rather than clinical symptoms in an attempt to get answers in a shorter time frame, one year versus several years. Dr. Porter commented that, "NAC will not be a cure by itself. We need to have some rational way to put various 'downstream' therapies together so that each impacts a specific pathological process. The ongoing animal research will give us an idea if we are impacting neurological symptoms and disease progression. In this case I felt we had a good rational, good markers and a drug with a good safety profile. That is why I pushed to get this trial running simultaneously with the animal studies." The data obtained from the NAC trial will also help in designing future trials, regardless of the efficacy of NAC.

Patients in the trial will have four visits to the NIH over 5 months. Subjects will be on NAC for 8 weeks and a placebo for 8 weeks. Potential candidates for the drug trial do not have to be participating in the Natural History Study. To qualify, NP-C patients are allowed to be on the drug Zavesca, although other supplements are not allowed. If you would like information about participating in this trial call Nicole Yanjanin, CPNP, at 301-594-1765 or email her at: nyanjanin@mail.nih.gov. Ms. Yanjanin has played a critical role in implementing and developing these clinical trials. Ms. Yanjanin's position is funded by the APMRF.

In addition to the drug trials with NAC, the Natural History study has shown some other promising research developments. When the study began, the major goals were: 1) to identify clinical or biochemical markers that can be used as an outcome measure in a therapeutic trial, to determine if a drug is affecting the disease process, and 2) to identify a test that could be used for diagnostic testing or screening.

Through this study a number of potentially promising protein biomarkers have been identified in cerebral spinal fluid from NP-C patients. Work is ongoing to determine if these protein biomarkers will be useful in future clinical trials. The NIH researchers are using the same oxysterol markers, but for two different purposes, as a biomarker outcome measure for the clinical trial and as a potential blood-based diagnostic test for NP-C.



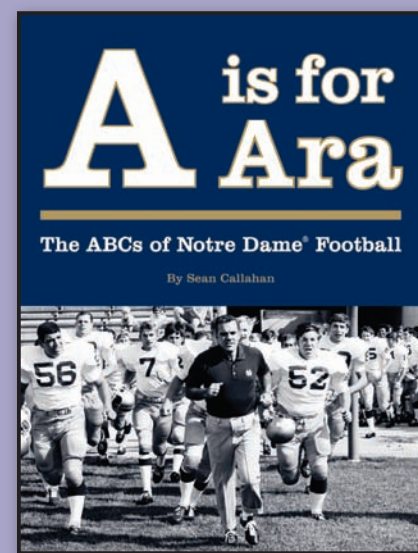
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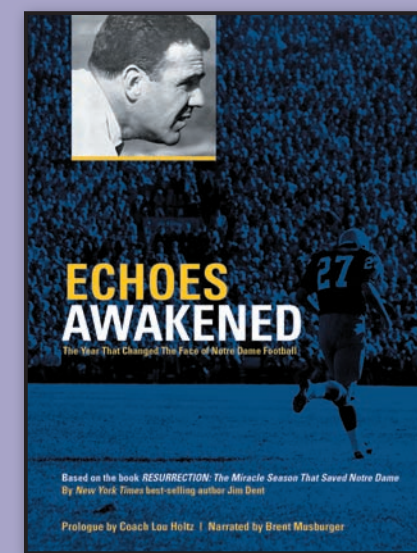
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Gift Giving Ideas for Notre Dame Fans!

Proceeds from the purchase of these items benefit the APMRF!



A is for Ara, The ABCs of Notre Dame Football by Sean Callahan. The perfect primer for Notre Dame fans, young and old! Special Ara Parseghian autographed copies available! Go to: www.aisforara.com



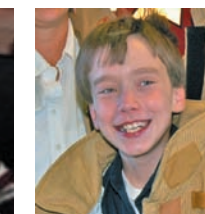
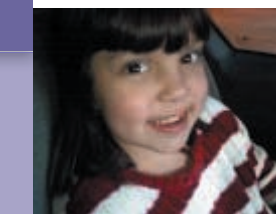
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A GOAL FOR LIFE

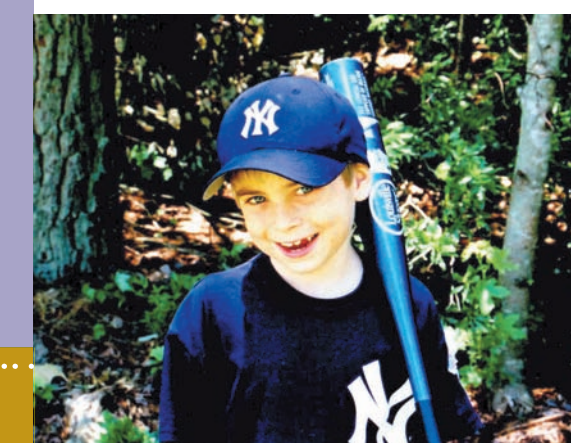
For Friends and Supporters of the Ara Parseghian Medical Research Foundation



*"If the only prayer
you said in your
whole life was,
"thank you", that
would suffice."*

—Meister Eckhart

From all NP-C children and their families we thank you for your support during this holiday season.



A Worthy Cause



Ashton Friedl with Aunt Sarah and Uncle Kevin Currie.

"It Comes In Pink" is the perfect name for a worthy cause....

Ashton Friedl is a beautiful, fun-loving 7 year old girl who lives in Mechanicsville, Virginia and has NP-C disease. Her friends at school and throughout their community have rallied around Ashton and her family to raise funds and awareness for NP-C.

On October 9th, the event *"It Comes In Pink"* took place...food, fun and a Motown Band rounded out the festive evening. Kevin Currie, Ashton's uncle, has enthusiastically worked over the past 6 months to make this event a reality which raised \$15,000 for NP-C research.

The event's title, *"It Comes In Pink"* evolved from a comment that Ashton made when faced with

the prospect of needing a cane to aid her walking. Her "Nana" feeling saddened over the image of the traditional cold gray metal variety was assured by Ashton that this clearly was not going to be a problem; with a big grin and a sparkle in her eye, Ashton exclaimed *"Nana, it comes in pink!"*

Cox Communications – Leader in Philanthropy

What do you get when you put together one of the most giving companies in the country with a dynamic leader dedicated to her community? The result is a winning combination that supports many worthwhile causes, including the race to find a cure for NP-C.

When Lisa Lovallo took over the reins as vice president and systems manager of Cox Communications of Southern Arizona, the entire Tucson region benefitted from her drive to improve the quality of life for those her company serves.

In 2006, Cox Communications joined the Parseghian Foundation with their support and participation in the annual "One More Victory, Ara!" event. Since 2008, under the leadership of Ms. Lovallo, Cox has played a major role as a Corporate Sponsor for this event.

The APMRF has come to realize and appreciate the incredible involvement that Cox Communications has with our Foundation and with the Tucson community. Their dedication to making Southern Arizona a better community is in evidence through the many partnerships they have developed with community organizations to aid and promote critical messages to the public.

Cox Communications invests in hundreds of non-profits organizations each year. In just Southern Arizona last year, more than \$1 million dollars were contributed by Cox to many worthwhile charities. Cox was instrumental in saving the Tucson International Mariachi Conference and the July 4th Tucson Fireworks. Cox also supports Primavera Foundation, Tucson Urban League, Big Brothers Big Sisters, El Rio Health Foundation and Chicanos Por La Causa, to name a few.

Many Cox employees also contribute their time and talents, holding positions on community boards and volunteering for many great causes on a regular basis. "Every single person from the manager level up sits on a non-profit board in our community," states Lovallo.

We applaud Cox Communications and Lisa Lovallo for their conscientious and thoughtful dedication to being fine role models for corporate philanthropy.



Lisa Lovallo and Cox Communications are great community supporters.

Heartfelt Thanks...

"Irish Legends"...Coaches Ara Parseghian and Lou Holtz are certainly that and these two legends are what inspired Skip Strzelecki and Jim Moriarity to create this event which has just completed its third year. Held at the Lost Dunes Golf Club in Michigan, this year's event was attended by two of Notre Dame's best...Heisman Trophy winners Johnny Lujack and Johnny Lattner. Friendships were renewed, memories shared and a beautiful summer day were the ingredients for success.

Funds raised at this event benefit both the Parseghian Foundation and the Lou Holtz Foundation. The Lou Holtz Foundation supports many worthy causes around the country including the APMRF. As in the words of Coach Parseghian, "I'm very grateful to the whole Notre Dame Family for supporting our foundation. The support we have received from not only the Notre Dame family but also the community has been terrific."

Many thanks to all who participated and especially to Skip Strzelecki, Jim Moriarity, Mike Leep Sr., Mike Nolan and Angela Monger for their ongoing enthusiasm and support in hosting this successful fun-filled tournament.



Lou Holtz, John Lujack and Ara Parseghian at the Irish Legends Tournament.



Keaton Smith with family and friends enjoying the event.

The *"BReak Thru Fund Golf Outing"*, hosted by the Smith family of Lafayette, IN was again a huge success. Hosted by Trent and Julie Smith in honor of their three children, Braden, Riley and Keaton, this event again raised significant dollars and awareness for NP-C disease.

This year's event held on August 15 included an 18 hole golf scramble, lunch and dinner/auction and was enjoyed by the many participants. The proceeds raised by the Smith Family's BReak Thru Fund support NP-C research at Purdue University.

The Notre Dame Club of Milwaukee hosted the ninth annual *"Ara's Outing 2009"* in Brookfield, WI this past July. More than a dozen from "The Era" travelled to Milwaukee to honor Ara. 150 alumni and friends – including 13 Irish football players from the period of 1964-74 – joined in the festivities at the beautiful Westmoor Country Club on Monday, July 13 to raise money for the Ara Parseghian Medical Research Foundation (APMRF). Standing in for the Hall of Fame coach who was unable to attend, alumna and daughter-in-law, Cindy Parseghian, the APMRF's president, thanked the attendees for the Club's nine years worth of contributions, saying that it has accounted for more than \$150,000 toward research to find a cure for NP-C.

The program followed an eventful day of golf and included speeches from some of the biggest names from "The Era of Ara", including: Nick Eddy '67, Pat Steenberge '73, and Art Best '76. Best, in particular, humored the crowd with stories of having landed in the Coach's office "no fewer than about 5,000 times" for various rules infractions. All speakers stated their unwavering appreciation for lessons instilled by Coach Parseghian. We wish to express our sincere thanks to Tom, Terry and Maggie Mulcahy for once again organizing a fabulous event that included a golf tournament, dinner and auction.



Ara's former players supporting the Milwaukee event.



Adam Recke and family.

"A good time was had by all" ...April 25 was the date of the **Race for Adam Foundation's** fourth annual *"2009 5k Run/Walk For A Cure"*. It was a beautiful spring day in Allentown, PA with over 700 participants joining Adam Recke and his family to help raise awareness and funds for NP-C disease. This is one of many events hosted by the Recke family each year.

What are you fighting for??...was the slogan for the 5k race, *"Running For A New Ara"* held on April 29 at the University of Notre Dame and sponsored by the College of Science and the Center for Rare and Neglected Diseases. Many thanks to John Markiewicz and Jenny Shin for their efforts to organize this event and to Riley Children's Foundation and St. Joseph's Regional Medical Center for their support.

Thank you again to all involved with the **"Pebble Beach Coaches Classic"** and to the many years of supporting the Foundation through this annual charity golf tournament. Coaches from around the country and their guests enjoy the beautiful Pebble Beach experience while raising funds for NPC. The Foundation is extremely honored to have been the beneficiary of this fine event for the past 6 years which has contributed over \$165,000 to the NP-C cause. Sincere thanks to Dick Tomey, Paul Spangler and Margo Daniels for their time and expertise.



Elise Barton



"Running For A New Ara"

Family and friends of Elise Barton, a precious 3 year old who was diagnosed with NP-C in 2008, hosted **"Hope On The Horizon"** on May 3 in Minneapolis, MN. This evening of fun and purpose raised more than \$34,000 to support NP-C research. For an insightful and touching glimpse into the life of this beautiful child visit: <http://www.youtube.com/watch?v=ReuyBhXsR9U>

Mark Your Calendar

November 20, 2009 – Tiffany & Co., La Encantada, Tucson, AZ is hosting **"Pearls For A Cause"**, a cocktail reception to benefit the APMRF. Buy a pearl and a chance to be a winner of a beautiful Tiffany & Co. pearl torsade necklace. For more information contact Peg Romano: (520) 577-5106.

January 23, 2010 – Every January the local community of friends, benefactors and businesses in **Las Vegas, NV** come together to honor and support 12 year old Ty Quandt through

a benefit concert and silent auction called **"Touchdown for Ty"**. This year marks the fifth year of this fun-filled event. For more information go to: www.touchdown4ty.com or call Verna Burrows: (702) 363-5443.

April 6, 2010 – **"The Battle of the Bend, Silver vs. Gold Baseball"**. Next year's battle between the ND Fighting Irish vs. South Bend Silver Hawks will take place on April 6th at 5:30 pm, Coveleski Stadium. A portion of the proceeds to benefit APMRF.

May 14-15, 2010 – The 15th Annual **"One More Victory, Ara!"** **Celebrity Golf and Gala Weekend** presented by University Medical Center will take place at the beautiful Westin La Paloma Resort & Spa, Tucson, AZ. This will be a fabulous weekend of great golf, a splendid auction and a star-studded gala with wonderful entertainment! For more information or to make an auction donation contact APMRF: (520) 577-5106 or go to www.parseghian.org.