Familial Amyotrophic Lateral Sclerosis
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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative condition characterized by the progressive deterioration of motor nerve cells (neurons) in the brain and spinal cord. These motor neurons, which initiate and control muscle movement throughout the body, slowly degrade over time until they are no longer functional. ALS is predominately a sporadic disease, meaning that most individuals with ALS are the only person in their family to develop the disease. Approximately 10% of individuals with ALS have a close family member with ALS; this is known as familial ALS (FALS).

Genetics 101

Our genetic material, called DNA, is stored in every cell of our body and packaged into chromosomes. Most individuals have a total of 46 chromosomes. Chromosomes come in pairs, and in each pair, one chromosome comes from the father and one chromosome comes from the mother. The first 22 pairs of chromosomes are the same in males and females (known as autosomes), whereas the 23rd pair determines our sex (males, XY and females, XX).

Each chromosome is made up of many genes. Genes are specific segments of DNA on a chromosome that carry the instructions for making proteins. Proteins are the building blocks for the body’s structure and function, and contribute to traits such as eye color. Because we have two copies of every chromosome in our body, we have two copies of every gene. A mutation is a permanent change in the DNA. When there is mutation in a gene, the gene may not be able to correctly make the protein and this may lead to disease.

There are two patterns in which familial ALS can typically be inherited: autosomal dominant and autosomal recessive. “Autosomal” refers to the first 22 pairs of chromosomes, which are identical in both males and females. Therefore, both genders have an equal chance of being affected.

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Autosomal Dominant Inheritance

In this form of inheritance, having a mutation in only one copy of a gene can cause an individual to develop the condition. Typically, the copy of the gene with the mutation is inherited from a parent, and most individuals with an autosomal dominant disease will have a family history of the condition. Children of a person with a dominant mutation have a 50% chance of inheriting the copy of the gene with the mutation and a 50% chance of inheriting the copy of the gene without the mutation.

Autosomal dominant genetic diseases cannot skip a generation. However, there are several reasons a genetic disease may appear to skip a generation, even though the mutation does not skip a generation. For example, sometimes an individual may pass away from an unrelated cause before ever developing symptoms of the disease. Also, some mutations do not always result in disease because of a genetic concept known as reduced penetrance. In both of these scenarios, the person carrying the mutation can still pass it on to the next generation.

Autosomal Recessive Inheritance

In autosomal recessive inheritance, a mutation in both copies of a gene is necessary in order for an individual to develop the condition. Typically parents of an affected individual do not have the condition themselves, but are carriers for the mutation. Carriers are individuals who have one copy of the gene with the mutation and one copy of the gene without the mutation. When two carriers have a child, there is a 25% chance the child will inherit both copies of the gene with a mutation and develop the condition. In most cases of autosomal recessive disease there is not a family history of the condition in previous generations because a single copy of a gene mutation may be passed silently through a family.

Familial ALS Genes

By far the most common pattern of inheritance for FALS is autosomal dominant. To date, 7 autosomal dominant FALS genes have been identified. SOD1 was the first FALS gene identified; mutations in the SOD1 gene account for 15–20% of FALS cases, and are highly penetrant, meaning that almost everyone with a mutation will develop symptoms of ALS. In 2006, TDP-43 was identified as the major disease protein present in the motor neurons in most cases of ALS at autopsy. Sequencing of the gene responsible for making the protein TDP-43 (TARDBP) revealed several mutations in both FALS and apparently sporadic ALS cases. Mutations in the TARDBP gene account for less than 5% of FALS cases and for 1–3% of ALS cases overall. In 2009, mutations in the gene FUS were identified as another cause of FALS, accounting for 3–5% of FALS cases. Mutations in the genes VAPB, ANG, FIG4, and SETX have also been reported to be rare causes of FALS.

ALS may also be inherited in an autosomal recessive pattern. The alsin gene has been identified as a cause of autosomal recessive ALS. Mutations in the alsin gene cause juvenile-onset ALS. Affected individuals typically have a slowly progressive form of ALS with onset of symptoms before 25 years of age.

ALS and FTD

Frontotemporal disease (FTD) is a type of dementia characterized by gradual and progressive changes in behavior and/or language dysfunction. Approximately 15% of individuals with ALS also have a clinical diagnosis of FTD. In addition, a number of families with a family history of both ALS and FTD consistent with autosomal dominant inheritance have been reported. Many of these families have been linked to a region on chromosome 9 but the gene responsible for the disease has not yet been identified. Mutations in the TARDBP gene have been identified in a small percentage of families with FALS/FTD.

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Genetic Testing

Genetic testing involves collecting a sample of blood or saliva. DNA is isolated from the sample and analyzed for mutations in the specific genes of interest. Clinical genetic testing is currently available to look for mutations in the SOD1, TARDP, FUS, ANG, SETX, VAPB, and alsin genes.

Any individual with ALS who is interested in genetic testing may get tested, though a genetic cause is more likely in those individuals who also have a family history of ALS or a juvenile-onset form of ALS. Anyone considering testing or who has a family history of ALS should seek genetic counseling prior to genetic testing. The goal of genetic counseling is to help people understand more about the genetic causes of a disease and how it may affect them so they may make informed decisions. Genetic counselors can explain how genetic conditions are inherited, determine if an individual is at risk, provide options and guidance, and find referrals for other resources.

Genetic testing is most beneficial when a family member with ALS is the first person tested. Once a mutation has been identified, other members of the family may choose to be tested for the same mutation even if they don’t have symptoms of the disease.

There are three possible types of genetic test results: positive, negative, and indeterminate. A positive test result would mean that the individual has a disease-causing mutation in the gene tested. A positive test result indicates that the cause of ALS has been found and would further define the risk for other family members to develop ALS. A negative test result would mean that the individual did not have a mutation in the tested gene or genes. However, a negative result would not completely rule out the possibility of a genetic cause of ALS, because there are likely other genes associated with ALS that have not yet been discovered. An indeterminate result means that a change was found in the genetic sequence of the gene, but the laboratory cannot yet make a clear determination as to whether it is a disease-causing mutation or not. It is important to have a genetics professional review and explain the genetic test result with the patient and family to ensure that an accurate interpretation of the result is provided.

Sporadic ALS

Sporadic ALS is believed to be caused by a complex interaction between multiple genetic and environmental factors and aging. However, to date no single gene has been consistently shown to be associated with an increased risk of ALS.

There is still much to learn about the genetics of both familial and sporadic ALS. The knowledge gained from genetic research will lead to better insights into the cause of ALS and will help guide the development of new therapeutic strategies.

If you would like further information, please contact either Dana Falcone at the University of Pennsylvania Center for Neurodegenerative Disease Research or a genetic counselor in your area. Ms. Falcone can be reached by email at cdana@upenn.edu or by telephone at 215-615-3226. To find a genetic counselor in your area please visit www.nsgc.org.

Upcoming Events

► 2010 Lehigh Valley Walk to Defeat ALS® - 10/23/10
► Newly Diagnosed – Ambler - 10/25/10
► 2010 Greater Philadelphia Walk to Defeat ALS® - 11/6/10
► Nurturing the Nurturer - 11/7/10
► Holiday Party - 12/5/10

Please note: Advance reservations are required for all events.
Contact the Chapter Office for additional information - 215-643-5434.
Why Should You Be A Part of the Walk to Defeat ALS®
Allison Walker, Events Manager

There are so many reasons to be a part of the Walk, from connecting with people who are already a part of the ALS community to making a difference to helping the cause.

We asked Jacqueline Young, team captain of Bo Peep’s Fantastic Sheep in the Harrisburg Walk and Dawn Spence, team captain of Donna’s Dugout in the Lehigh Valley Walk why they walk.

We walked this year in honor of my mother, who was diagnosed with ALS in 2009. It was such a devastating diagnosis for all of us, and we felt the walk was one way to rally support from friends and family in Mom’s fight against ALS. The walk was such a positive and uplifting experience. We had almost 60 friends and family walking with us. It is so comforting knowing that so many people are there to support us; not just with the walk, but in the challenges we face on a daily basis. In addition, Mom has benefited so much from the ALS Association, and the walk was an opportunity to give back to such a supportive organization. We found it very easy to get involved as a first time team. Starting about a month before the walk, we rallied friends and family through e-mail and word of mouth. We found it incredible that we raised over $6000 in such a short period of time!

I walk for Donna; my sister and every other PALS (person with ALS) that I have met personally or read about their journey with ALS. They all inspire me in the strength that they put forth in dealing with the lifestyle changes that they have been handed when the diagnosis of ALS was given. I guess I am a dreamer and that is also why I walk. I dream of the day that the treatment and cure of ALS is available and we will no longer need to talk about how ALS changed Donna’s life, or your loved one’s life. I never did well in Science classes in school, so I am not the research scientist that will come up with the miracle breakthrough, and I have not hit the lottery yet to fund all of that research by myself, but I can make my contribution and join the Walk and feel like I am doing what I can to help The ALS Association fund the research and deliver all of the patient services that they provide. These programs can’t happen unless you and I make the effort and help.
November is National Family Caregiver Month

FOUR MESSAGES TO LIVE BY

(Adapted from the National Family Caregivers Association, http://www.thefamilycaregiver.org/)

Becoming a family caregiver for someone you love may involve heart wrenching and at times enlightening life lessons. These journeys become a part of us and make us who we are. We are here to learn from one another, and through these lessons, we can heal our relationships and sometimes ourselves.

Your role as a family caregiver can happen abruptly or creep in slowly, unnoticed, until one day, you realize you are caring more for someone else than you are for yourself. In dealing with ALS, your new role as a family caregiver can feel as overwhelming as the initial diagnosis of ALS in your loved one.

Believe in Yourself: Try to maintain a positive attitude by recognizing your strengths and limitations. No one begins caregiving as an expert from the beginning; it takes time and experience, exploration, and many mistakes and little victories as you learn “on the job.” Remembering and appreciating the strengths you bring to the table will go a long way in your ability to set goals and healthy boundaries, for yourself, and for your loved one.

Protect Your Health: It is critically important to maintain your physical and emotional health and well-being: if you don’t, who will? Your good health is the greatest gift you can give your loved one and your entire family. You may not be able to do this easily, especially if guilt tends to get in your way; but it is vital that you try. “Have patience with all things, but chiefly have patience with yourself.” (St. Francis de Sales) You may want to repeat this quote to yourself in those challenging moments! In addition:

- Take a daily vitamin supplement
- Get exercise -- make it a priority for both your mental and physical well-being.
- Get regular check-ups and do not ignore possible symptoms of ill health.
- Get a flu shot
- Take a break from caregiving -- respite time is crucial. Ask your ALS Social Worker about caregiver respite support from the Chapter.
- Stay involved in hobbies- adapting them for your new situation
- Laugh with a friend

Watch for signs of depression. A family caregiver suffering from major depression experiences a combination of at least five of the following for at least a 2-week period:

- Depressed mood, loss of interest or pleasure in most daily activities
- Significant change in weight or change in appetite
- Trouble sleeping or excessive sleeping
- Feeling tired and a lack of energy
- Feelings of hopelessness and helplessness
- Feelings of worthlessness, self-hate, and inappropriate guilt
- Feelings of low self esteem
- Sudden outbreaks of anger
- Difficulty in thinking, concentrating or making decisions
- Recurring thoughts of death or suicide

Reach Out For Help: reaching out and asking for help is never a sign of weakness, rather it demonstrates determination, an awareness of your own abilities, and a strong sense of self. Talk to your ALS Mental Health Nurse and Social Worker, reach out to a clergyperson you trust, family and friends. Attend a Caregiver Support Group through the ALS Association or other organizations.

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**Speak up for your Rights:** The ALS Association is keenly aware that more help is needed for caregivers in the home. Currently, the National ALS Association joined with other organizations for the passage of a National Respite Care Act, with state funding to support local respite care programs (such as the Philadelphia Chapter’s) available to people with ALS and other diseases. Pennsylvania, New Jersey and Delaware have not received Respite Care Act monies—yet! We’ll know more about future funding this fall, and meanwhile, the ALS Association is lobbying at the national level for increased funding for 2011 as well. To voice your support for this and other important legislation, or to ask others in your web of caring friends and family asking “What can I do?”: sign up for “Action Alerts” under the “Public Policy” link at www.alsa.org.

We must accept finite disappointment, but never lose infinite hope. (Martin Luther King)

♥ In celebration of the fabulous caregivers in our midst, we recognize National Family Caregivers Month! ♥

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**Absentee Ballots – Voting in the General Election**

If going to the polls to vote in person is a hardship because of your disability you are eligible to vote via an absentee ballot. You should consider getting the application as early as possible.

In Pennsylvania, you may obtain an absentee ballot request form on line at http://www.longdistancevoter.org/pennsylvania
You can also pick up this request form at the County Election Bureau office in your county.

In NJ, anyone can vote by Absentee Ballot. You can download the absentee ballot request at http://www.longdistancevoter.org/new_jersey or get a form from the County Clerk Office in your county.

In Delaware, you may download the affidavit form at http://elections.delaware.gov/services/voter/pdfs/absentee.pdf or get the form at the Department of Elections in your county.

If you have any questions about the location of the appropriate county office in your state, or need assistance to make sure that you can exercise your right to vote, please contact one of the social workers at the ALS Association.

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**Vision Statement:**

The vision of The ALS Association, Greater Philadelphia Chapter, is a world free of Amyotrophic Lateral Sclerosis (ALS).

**Mission Statement:**

Leading the fight to treat and cure ALS through global research and nationwide advocacy while also empowering people with Lou Gehrig’s Disease and their families to live fuller lives by providing them with compassionate care and support.