

APBDRF

A d u l t
Polyglucosan
Body Disease
R e s e a r c h
F o u n d a t i o n



Newsletter No. 2 April 2008

Our Mission

The Adult Polyglucosan Body Disease Research Foundation (APBDRF) is the only national non-profit health organization dedicated solely to finding the cause and cure for Adult Polyglucosan Body Disease (APBD). APBDRF strives to be the leading charitable funder and advocate of research worldwide.

Our mission is to improve the diagnosis and treatment of APBD, support individuals and families affected by the disease, increase awareness of APBD among health professionals and the public. Our ultimate goal, and the heart of our program is to find the underlying cause as well as a cure for APBD and its complications through the support of research, education, and patient services.

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Message from the Director



Gregory Weiss

Happy New Year and welcome to the second newsletter of the Adult Polyglucosan Body Disease Research Foundation (APBDRF). We are the only national non-profit Adult Polyglucosan Body Disease (APBD) organization.

Our mission is to improve the diagnosis and treatment of APBD, increase awareness of APBD among health professionals and the public, and support individuals and their families affected by the disease.

We are also striving to identify the underlying causes as well as a cure for APBD and its complications by supporting research, education, and patient services.

I am very enthusiastic and excited that APBDRF is funding its first research projects. This is an important time for the APBDRF community. I want this accomplishment to provide momentum for getting the word out about APBD and the foundation's work.

If you are a person with APBD, know someone with this disease, or a family member of someone with this disease, we invite you to contact us to learn more about the APBDRF. Call us 212-290-2546, email us info@APBDRF.org, or visit our website at www.APBDRF.org.

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Medical Advisory Committee

The Foundation's Scientific/Medical Advisory Committee is comprised of respected researchers and practitioners knowledgeable about APBD and similar disorders.

From the outset of our quest for answers about APBD, our medical advisory board has provided professional advice and encouragement for all our efforts. They have always been thoughtful, caring and compassionate, even during discouraging times. Their guidance has been invaluable. The advisory panel is a vital part of our Foundation, and we are grateful for the commitment, time and expertise the members so graciously provide.

H. Orhan Akman, PhD

*Research Scientist at H. Houston Merritt Research Center
Columbia University*

Salvatore DiMauro, M.D.

*Professor of Neurology
Director of H. Houston Merritt Clinical Research Center
Columbia University and Columbia Presbyterian Medical Center*

Christopher Klein, M.D.

*Department of Neurology
Mayo Clinic*

Edwin Kolodny, M.D.

*Professor of Neurology
Chairman, Department of Neurology
New York University School of Medicine*

Alexander Lossos, M.D.

*Department of Neurology
Hadassah University Hospital, Jerusalem, Israel*

Douglas C. Miller MD, PhD

*Clinical Professor of Pathology and Anatomical Sciences
University of Missouri School of Medicine*

Berge Minassian, M.D.

*Research Scientist
The Hospital for Sick Children, Toronto University*

Gregory M. Pastores M.D.

*Associate Professor, Neurology
New York University Medical Center*

Raphael Schiffmann, M.D.

*Director, Institute of Metabolic Disease
Baylor Research Institute, Dallas, TX*

Sara Shanske, PhD

*Research Scientist at H. Houston Merritt Research Center
Columbia University*

Thomas M. Wisniewski, M.D

*Professor of Neurology
New York University School of Medicine*

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A letter from Dr. Alexander Lossos

Dr. Alexander Lossos, of Hadassah University Hospital in Jerusalem, Israel, is one of the leading authorities in the field of APBD. Dr. Lossos discovered the biochemical defect (glycogen branching enzyme deficiency) in 1991 and the genetic mutation (Tyr329Ser) in 1998 in patients with Adult Polyglucosan Body Disease (APBD). Dr. Lossos has the largest population of APBD patients under his care.

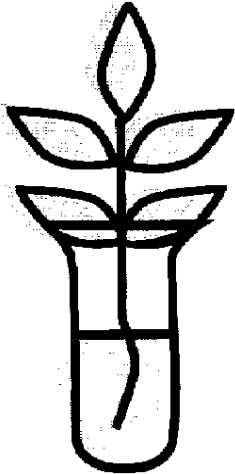
Since the early recognition of APBD as an independent clinical-pathological entity in 1980, significant progress has been made in our understanding of this devastating disorder. Biochemical abnormality was demonstrated in 1991 and genetic defect was identified in 1998. Dysfunction of the glycogen branching enzyme (GBE) related to mutations in the GBE gene underlies the accumulation of abnormal polysaccharide in the nervous system causing progressive symptoms and signs of the disease. Today these findings enable easy and reliable diagnosis for the patients as well as appropriate genetic counseling for the families.

However, much still remains unknown. We still do not know why some patients with APBD do not show the typical laboratory findings, why similar laboratory findings may be associated with different clinical manifestations, and what causes the selective tissue vulnerability and late clinical onset in APBD. Even more importantly, we still do not have effective therapeutic options for the patients with this relentlessly progressive disease.

The Adult Polyglucosan Body Disease Research Foundation, (APBDRF) established in 2005, marks the most significant change in current and future APBD research. With the aim of improving knowledge about the disease, increasing awareness among the professionals, and supporting the individual patients and their families, APBDRF is responsible for the unique momentum of multi-center, international clinical and scientific effort to solve the puzzle of APBD. Involved institutions are dedicated, world-known medical centers that will focus on the clarification of genotype-phenotype relations, production of an appropriate animal model, and development of effective treatment using sophisticated clinical and scientific methods. I personally, and the APBD community in Israel are proud and excited to be part of this promising momentum.

Alexander Lossos, MD
Hadassah Medical Center, Jerusalem, Israel
January 19, 2008

Basics on APBD



While fundamental symptomatic information about (APBD) is somewhat widely available, such as the presentation of APBD in individuals age 50 and over, its attack of upper and lower neurons, sensory loss, early neurogenic bladder, and in some cases dementia, (H. O. Akman, PhD), patients, families, and the medical community are often less familiar with scientific explanations of this disease.

H.O. Akman, PhD (Columbia University), Dr Berge Minassian, MD-University of Toronto, and M. Tropak, PhD (Toronto University) have provided the APBD Research Foundation with short explanations of APBD and their research efforts. Their statements are below.

What is APBD?

APBD is a devastating neurological disorder robbing its victims of their ability to walk, speak, think and function normally. It is caused by a mutation of the glycogen branching enzyme gene, which results in the accumulation of masses of abnormal glycogen, called polyglucosans that are starch-like in nature and thus insoluble. These polyglucosan bodies accumulate in the axons of brain cells. The axons are the long electrical threads that conduct messages from the brain to the rest of the body. The starch-like polyglucosan material blocks the axons resulting in the malfunction that characterizes this disease.

A more scientific explanation is as follows:

Patients with APBD have high levels of "polyglucosan" in their cells. This abnormal form of glycogen has less branching points and longer peripheral chains and is less soluble than normal glycogen. Due to a mutation in the gene for the glycogen branching enzyme (GBE), the GBE, does not work properly. GBE like other enzymes is a protein that consists of a long "string" of amino acids. As this "string" is being made, it must "fold up" into the right shape in order for the enzyme to become functional. It is believed that in some patients with APBD a specific amino acid is changed and the mutant form of the GBE protein has difficulty in either reaching or maintaining its shape. Therefore, there may not be enough functional GBE to properly do its biological job (i.e. to branch the glycogen). This results in a less branched glycogen that is not as soluble as it should be which then accumulates.

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Advances in Research on APBD

What is the focus of research on APBD?

Development of a mouse model:

Dr. Akman (Columbia University) reports that in order to better understand this disease and to test therapeutic strategies, an animal model would be very valuable. The American quarter horses and Norwegian forest cats are two naturally occurring models of this disorder, but due to their impracticality as laboratory animals, Dr. Akman and colleagues

propose to develop a mouse model of APBD, to increase understanding of the pathogenesis of the disease and to test therapeutic strategies aimed at increasing the residual activity of branching enzyme in tissues.

Curing APBD by eliminating the polyglucosan bodies:

Dr. Minassian (University of Toronto) has proposed that the cure for the disease will come from unclogging the axons, i.e. melting away the polyglucosans. The only natural way to digest starch-like materials is by enzymes called amylases. This is how humans, for example, digest the starch they eat. Amylases are secreted into saliva and into the intestines to digest starch eaten as part of food. In APBD, the abnormal starch accumulations are inside the brain cells. No human cells make amylases within cells. All human amylases are secreted into the mouth or gut.

Dr. Minassian (University of Toronto) will engineer a mouse that will produce amylase in its brain cells. Columbia University will make a mouse model of APBD which will have polyglucosan bodies in their brain cells. They will then breed their neuronal amylase-producing mice with the APBD mice, thus transferring the amylase-producing trait to the APBD mice. Now, the APBD mice will make amylase in their brain cells. The amylase will adhere to the abnormal starch (polyglucosan bodies) in the APBD mouse brain cells and immediately digest it. The axons will be free to conduct normally and the mouse will be cured. The production of amylase in these engineered mice is controllable, i.e. they will produce amylase only on demand, and thus the amylase will be present to do its job only briefly until the starch is cleared. The purpose of this experiment is to prove that amylase introduced into brain cells of APBD models can clear the starch and can cure the mice.

Development of a Pharmacological chaperones for human GBE mutants:

Dr. Tropak (University of Toronto) explains that the amount of mutant protein can be increased to reach the right shape by adding a drug that binds to those enzymes that have already reached the right shape. This drug may act by "steering" any GBE proteins that are being made in the right direction resulting in proteins with the right functional shape.

Dr. Tropak and his colleagues will determine which of 3000 drugs that have already been tested in humans can specifically bind to and stabilize normal GBE. Once this chemical is found, they plan to treat skin cells from patients with APBD and determine whether this drug can increase the amount of mutant GBE that can function properly. They then plan to determine if the compound is toxic and whether it works in mice with a similar disease.

Living with APBD: Patients Share their Experience

Four patients recently took the time to share their experiences of living with APBD with our organization. From their experiences a picture emerges a picture of the struggles that many APBD patients confront everyday. Indeed, it is evident that APBD impacts on virtually every aspect of daily living and may also require the patient's dependency on others.

Two of these individuals live in the United States, one in Argentina and one in Israel. Of these four people, three are in advanced stages of the disease and one walks without ambulatory aids but experiences gait and balance issues. All four individuals reported bladder problems, frequent visits to urologists and many self-catheterize. They also reported that they must pay close attention to diet, especially to monitoring their sugar intake. The average monthly cost of care reported by these individuals ranged from \$200 to \$1,200 dollars a month. This includes doctor visits, physical therapy, medication, and cost of ambulatory aids (e.g. walkers, scooters).

Ms. Z, 57 years of age, reported being tired a great deal of the time, explaining that "this tiredness is invasive. It interferes with my ability to be spontaneous. I have to organize my schedule based around when I get tired. I feel old." Ms. Z also contemplates her future: "I don't want to become a burden on my children. I want them to lead their lives and not have to worry about me."

Mr. R noted, "It is difficult knowing that I cannot take long walks on the beach and in the woods. Bladder problems also limit my mobility to go very far from home for very long."

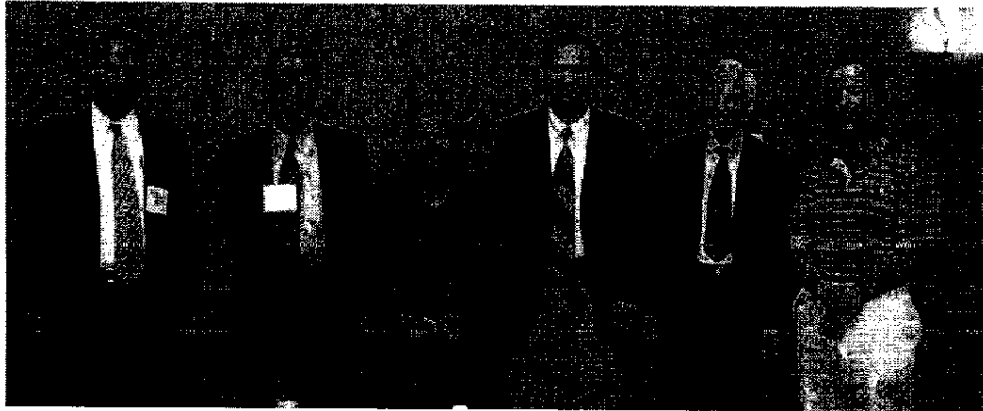
Mr. G, in his 70s reports, "I have lost my mobility, my ability to walk and to stand. You become so very dependent on your fellow man to assist you in your everyday life. I thank God for the people in my life who help me... without them I would not be able to work. And I am blessed with a very special wife who takes such good care of me, allowing me to lead as normal a life as is possible."

In sum, as APBD progresses, the environments of those suffering from this disease become markedly limited physically, socially and economically. Therefore, in addition to finding a cure or treatment for APBD, our foundation is committed to helping individuals suffering from this disease and their families cope and live the best life possible.

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APBD participation in the 59th Annual American Academy of Neurology

APBDRF's participation in the 59th Annual American Academy of Neurology (AAN) Expo in Boston April 30 – May 3, 2007 was successful. We increased awareness about APBD in the medical community and were represented by many members, supporters, volunteers, researchers and medical professionals who have made significant commitments to our cause.



Medical Advisory Board at 2nd Annual APBDRF Conference in Boston, MA April 30, 2007.

Upcoming Event!

We look forward to exhibiting at AAN 60th annual conference/expo in Chicago, IL Monday April 14th to Thursday, April 17th, 2008! At the conference, Monday, April 14th scientists will be meeting for the APBDRF's 3rd International Scientific/Medical conference from 12pm to 4pm. This meeting is open to patients, families, and medical professionals and will address updates on research and summaries on ongoing research studies as well as related medical advances. The APBDRF will also be exhibiting during the conference and will be located in the McCormick Exhibition Center – Booth 228-B. If you are a medical professional interested in attending the conference, see the Annual American Academy of Neurology website for information and registration at <http://www.aan.com/go/am>. If you are interested in volunteering and attending with APBDRF, please contact Gregory Weiss at Gregory@apbdrf.org or call 212 290 2546.

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APBD Quick Facts

Signs and Symptoms

- Over 40 years of age.
- Walking difficulty (including numbness, tingling in legs/toes), neuropathy.
- Neurogenic bladder.
- Brain white matter changes.

The Genetics of APBD

- Autosomal recessive.
- Many patients are of Ashkenazi Jewish ancestry.
- Half of patients have deficiency of glycogen-branching enzyme.

Clinical Findings

- Severe weakness, leg stiffness.
- Deterioration in gait, poor balance.
- Distal sensory loss in the lower limbs.
- Urinary dysfunction, incontinence.
- Impairment in executive functions and cognition.

Current Treatments

- Supportive with symptomatic care.
- Bladder care with anticholinergic agents (medication) and self-catheterization.
- Ambulation aids.

Resource List for Patients and their Families

For a more comprehensive list of resources, please see our website at www.APBDRF.org

National Tay-Sachs & Allied Diseases Assoc., Inc.

1700 14th St. N.W.

Association for Neuro-Metabolic Disorders

10000 Rockledge Drive, Suite 100

Tel: (419)885-1497

National Institute of Neurological Disorders and Stroke (NINDS)

Tel: (800)352-9424

10 Convent Drive

Genetic Alliance

1000 17th St. N.W.

The Association for Glycogen Storage Disease

1000 17th St. N.W.

National Family Caregivers Association

1000 17th St. N.W.

Aging Parents and Eldercare

1000 17th St. N.W.

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Career Opportunities at APBDRF

Adult Polyglucosan Body Disease is a fatal, neurodegenerative disease that attacks nerve cells and pathways in the brain. Our mission is to fund research that can one day find a cure for this disease that primarily affects Jews of European descent.

The Adult Polyglucosan Body Disease Research Foundation (APBDRF) was formed in 2005; a start-up grassroots non-for-profit organization founded by Gregory Weiss. Please see our website at www.apbdrf.org to learn more about us. The following internship and job positions have become available. If interested please send your resume and cover letter to info@apbdrf.org or fax it to 212-643-0963.

Job Posting: Grant Writer

Part-time (20 hours/week) Grant Writer in our development office. The primary function of this position is to research new funding opportunities, write and develop grant proposals for private corporate and foundation prospects, and develop strategies/relationships to increase support from corporations, foundations, and other grant-making organizations.

Responsibilities

- Work closely with executive director and development consultant.
- Develop prototype grant proposals.
- Create a tracking system acknowledging preparation of compliance reports, budgets and maintenance of records, track cultivation efforts and applications for funds.
- Work with development consultant to produce fact sheets, news releases, and related materials highlighting grant activities.
- Conduct research to identify new sources of corporate, foundation and grant support.

Qualifications

- The ideal candidate will have: Bachelor's degree and at least two years of experience.
- Possess highly developed writing and presentation skills.
- Proficiency in Microsoft Office computer programs
- Excellent writing skills.
- Demonstrated ability to promote orally and in writing, complex goals, strategies, and legal concepts in clear, accessible form.
- Must be able to work independently.
- Strong organizational skills, attention to detail and ability to meet deadlines ability to conduct research and report on outcomes.

Internship Available: Intern coordinator

Part-time (10 hours/week) intern in the development office. The foundation is seeking a responsible, organized intern with a passion for learning and making a difference.

Responsibilities

APBDRF is flexible in the creation of the internship position. Some duties would include:

- Making phone calls/Sending eMails.
- Volunteer recruitment.
- Coordination of board meetings.
- Research target organizations and companies.

Qualifications

- Candidates must have strong writing skills and proficiency in Microsoft Word and Excel.

Additional Information

Locations: New York
 Openings available: 3
 Salary: Unpaid
 Duration: 3-6 months

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We need your help! We need volunteers!!

Building up a foundation is not easy, searching for the treatment or prevention on APBD is not easy, increasing awareness on APBD is not easy, but we can do it if you help us, if your community or family helps us. Please help us!!

Ways You Can Help

Providing education and resources about testing and supporting research to help prevent APBD requires funding and collaboration. The APBDRF can only continue to make a difference in dealing with this deadly disease with your help. This help can come in the form of tax-deductible contributions, volunteering or as part of our local and national outreach efforts.

Help Spread the Word

- ✓ Our efforts to build awareness can only be accomplished with your assistance.
- ✓ Please let us know about APBD families in your community.
- ✓ We need you to spread the word about screening and prevention to individuals and families through your synagogues, local organizations and businesses, friends and healthcare providers.
- ✓ We need you to refer others to our Foundation and other appropriate sources about APBD.
- ✓ We will provide you with brochures and other literature for distribution and discuss setting up local chapters of the APBDRF in your area.

Conquering APBD requires collaboration, cooperation and commitment. Please help us to help you!

Your donation can start making the difference...

Your support makes it all possible!

To Make a Donation:

1. **Donate online on our webpage**
2. **Donate by Telephone**
Call the Foundation at the following phone number: 1-212-290-2546
3. **Donate by Mail**
Send your contribution to:
APBDRF
8 West 37th Street, Suite 901
New York, NY 10018
The Foundation is a 501 (c)(3) non-profit, tax-exempt organization designated by the Internal Revenue Code. Our federal tax identification number is 20-3609790.

Join Our E-mail List

E-mail us at info@apbdrf.org to so we can keep you posted about new developments and events. This list is for the APBDRF use only and will never be shared with anyone else.

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Other ways you can help

Your help can come in the form of tax-deductible contributions, volunteering your time as part of local or national outreach efforts, making presentations to companies, updating the website, working on our newsletter, and assisting in fundraising events!

If you are interested in becoming a volunteer, please complete and mail or fax the following questionnaire:

Name: _____

Specify your reasons for involvement with APBDRF: _____

How much time per week can you give to APBDRF?

Week Days: _____

Weekend: _____

In what way(s) are you willing to contribute?

- Financially**
- Volunteer**
- Make presentation to companies**
- Update the website**
- Work on quarterly newsletter**
- Assist in Fundraising events**

What is the best way to reach you?

- By Email:**
- By Phone:**

APBDRF

8 West 37th Street, Suite 901

New York, NY 10018

Phone: 1-212-290-2546

E-mail us at info@apbdrf.org