



## Porphyria DNA Testing Laboratory Established by the APF

A year ago, an anonymous APF member, recognizing the importance of gene testing for the seven porphyrias, provided a grant to the American Porphyria Foundation to support the development of a Porphyria DNA Testing Laboratory at the Mount Sinai School of Medicine in New York City. For the past year, Drs. Kenneth H. Astrin and Robert J. Desnick have been developing tests to identify the specific gene defects in each porphyria. These DNA-based tests are the most reliable way to confirm the diagnosis of a porphyria. Once the specific gene defect is known in a porphyria family, other family members can be accurately diagnosed from a blood sample.

Working together with the Porphyria Laboratory of Dr. Karl Anderson at the University of Texas Medical Branch in Galveston, Texas, the Mount Sinai Porphyria DNA Testing Laboratory already offers DNA-based testing for Acute Intermittent Porphyria (AIP), Congenital Erythropoietic Porphyria (CEP), and familial Porphyria Cutanea Tarda (fPCT). These DNA-based tests are only available to patients whose AIP, CEP or PCT has been confirmed by biochemical testing (either enzyme assays and/or measurement of urinary porphyrins and porphyrin precursors).

Patients should contact Dr. Kenneth Astrin at the Mount Sinai Porphyria DNA Testing Laboratory telephone: 212-659-6783 or [Kenneth.astrin@mssm.edu](mailto:Kenneth.astrin@mssm.edu) to inquire if they qualify for DNA-based testing and for information on sample requirements and shipping.

DNA tests for the other porphyrias, ALA, Dehydratase Deficient Porphyria, Hereditary Coproporphyrin (HCP), Erythropoietic Protophyria (EPP) and Variagate Porphyria (VP), are being established and patients with a confirmed biochemical diagnosis of these porphyrias are needed to provide samples for the development of these tests.

**1) Relevant Information for DNA Testing:** In each porphyria, there is a specific enzyme defect that results in the accumulation of the porphyrin precursors, ALA and PBG, and/or specific porphyrins. For example, in AIP, the level of

the enzyme porphobilinogen deaminase is half normal, and ALA and PBG accumulate, particularly during an acute attack. Similarly, in familial PCT, the level of the enzyme uroporphyrinogen decarboxylase is half-normal and a series of specific porphyrins accumulate in the urine, particularly when patients are symptomatic.

**2) DNA Testing:** Although each porphyria is due to a specific enzyme defect, it is now known that most families have different gene defects (or mutations) causing the defective enzyme. Thus, in each family, their specific gene defect can be found by determining its DNA sequence. DNA testing is more complicated and requires more time than measuring the levels of the enzymes or porphyrins, but once the specific gene defect is identified in a family, all family members can be tested to determine who has the porphyria-causing gene defect. For these studies, the DNA must be isolated from a small amount of blood sent overnight to the Mount Sinai DNA Porphyria Testing Laboratory.

**3) Free Testing for Biochemically Proven AIP, CEP and PCT Patients and their Families Until July, 2006:** Currently, the Mount Sinai Porphyria DNA Testing Laboratory is offering gene testing for AIP, CEP, and fPCT. Individuals who have biochemical evidence (enzyme assays and/or measurement of urinary porphyrin and porphyrin precursors) qualify for gene testing. You can arrange for gene testing if you have the results of the biochemical tests which can be performed by Dr. Karl Anderson's laboratory at the University of Texas Medical Branch in Galveston, TX (telephone Dr. Halberg: 409-772-4661) or through several commercial laboratories. Gene tests for AIP, CEP or fPCT will be provided for the next six months at no cost to you except for the blood drawing and shipping charges. After July 31, 2006, the cost of identifying a family mutation will be \$500 and then \$100 to test each family member. Typically DNA testing takes 2 to 4 weeks.

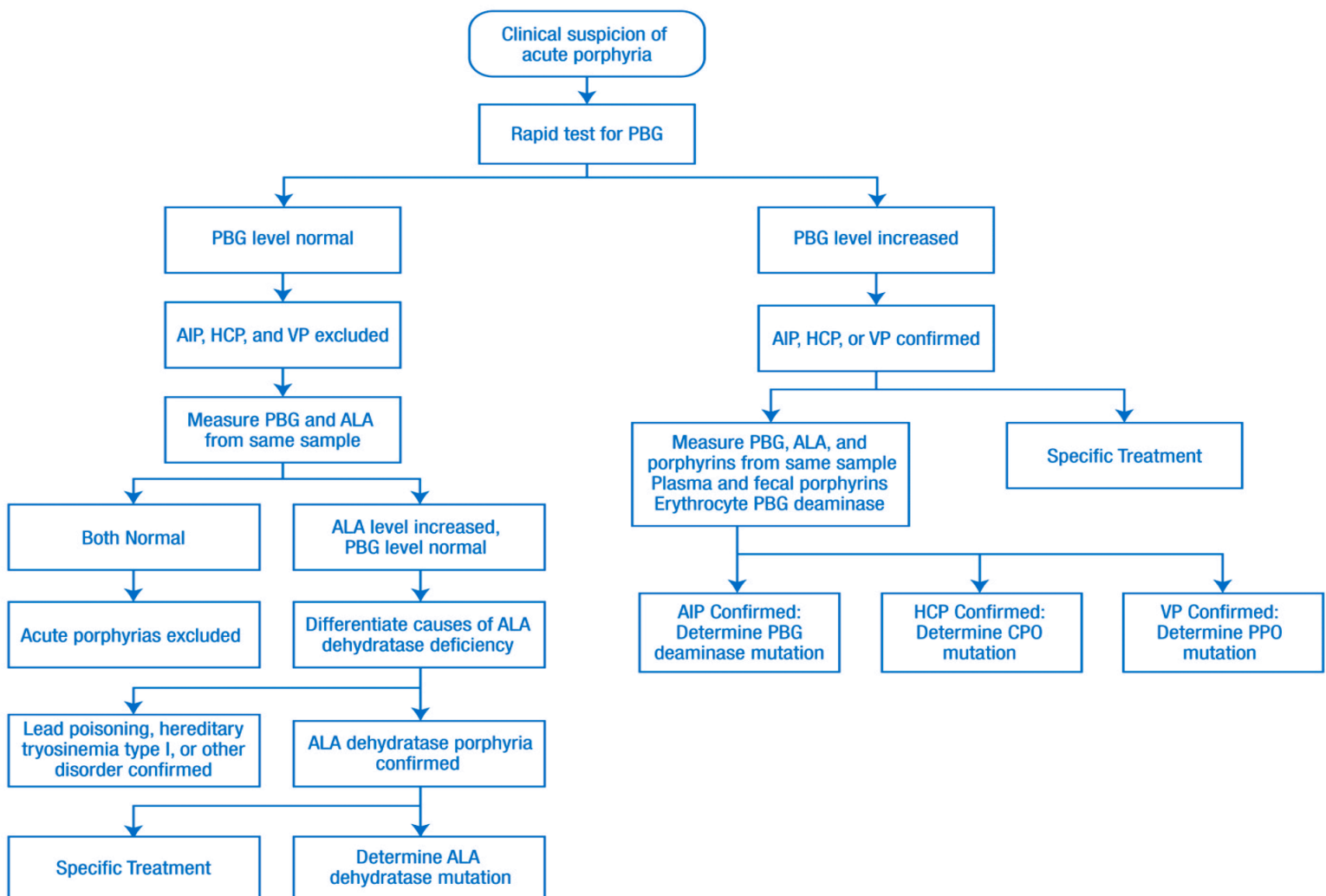
**Testing for Patients with Biochemically Proven HCP, VP and EPP:** If you have HCP, VP or EPP, the Mount Sinai Laboratory will determine your gene lesion as part of our efforts to establish these tests. Please contact the APF, who will inform you of the requirements for testing.

## Testing

Testing is one of the most misunderstood issues with the porphyrias, particularly the acute porphyrias. It is sometimes thought that testing and determining the results are different around the globe. However, testing is similar around the globe. For example, according to the Canadian Foundation site, "If a person is having an acute attack, their urine will always contain increased amounts of aminolevulinic acid (ALA) and porphobilinogen (PBG) which can be measured in the 'Watson-Schwartz' test. If it is suspected that you have abdominal pain or some other symptom due to acute porphyria, this test must be positive. If the porphobilinogen test is negative, some other cause for the symptoms must be sought."

We thank the European Porphyria Initiative for permission to use the following from their website [www.porphyrria-europe.org](http://www.porphyrria-europe.org). "In most patients with an attack of acute porphyria, PBG concentrations are at least ten times the upper limit of normal within one week of the onset of symptoms. PBG excretion decreases as the attack resolves. In AIP, excretion usually remains increased for many weeks but in VP and HCP may return to normal or near normal within a week or so after the onset of symptoms. If screening tests are negative and clinical suspicion of porphyria persists, it is essential to quantify uri-nary PBG and ALA, using a specific method, and analyze plasma and fecal porphyrins. If urinary PBG and ALA, plasma porphyrin concentration and fecal coproporphyrin III excretion is normal, acute porphyria is excluded as the cause of current symptoms. Enzyme measurements are not necessary for exclusion of porphyria as the cause of an acute illness and may give misleading information."

**The table below should help you understand screening for the acute porphyrias.**



## Porphyria Cutanea Tarda

Porphyria Cutanea Tarda (PCT) is the most common and most easily treated porphyria. It occurs worldwide in all ethnic groups and in both sexes. In PCT the activity of the heme synthetic enzyme, uroporphyrinogen decarboxylase (UROD) is deficient. Susceptibility to PCT is often inherited in which case the PCT is known as "familial" (type II). Reduction of UROD activity to approximately 25% of normal leads to the clinical expression of the disease

There is also a condition known as acquired PCT, which may occur in individuals with a genetic predisposition. In some cases, it is associated with hemochromatosis, another genetic disease in which there are excessive stores of iron. PCT generally begins in mid-adult life after exposure to certain chemicals that increase the production of porphyrins in the liver. These include alcohol, estrogen, iron overload, ethanol, polychlorinated aromatic hydrocarbons. like the dioxins, hepatitis and human immunodeficiency virus.

Since there is a deficiency of the enzyme which is a part of the process that transforms porphyrins and the other heme precursors into heme, the porphyrins are not being completely used. They accumulate in the liver and are transported to the skin by the blood plasma. Thus, when porphyrins are exposed to light and oxygen, they produce a charged, unstable oxygen which is harmful to the skin. Porphyrins accumulate in the liver and are transported to the skin by the blood plasma. The most common presenting sign is fragility of sun-exposed skin, leading to lesions typically on hands and forearms and occasionally on face or feet. Affected individuals may develop fragile skin, sores, blisters, and tiny cysts on the sun-exposed areas. They may also sunburn easily, have easily traumatized skin, develop mottled brown patches around the eyes, have increased facial hair and occasionally develop hardened skin on the neck, face and/or chest. Crusting and scarring of the skin can occur and generally takes a great deal of time to heal.

PCT can also cause liver damage, including liver cancer and cirrhosis of the liver. PCT has been associated with the development of hepatocellular carcinoma, chiefly in populations of older men with long-standing active disease, heavy ethanol intake, and cirrhosis.

PCT is diagnosed by testing the blood plasma, urine, and stool for porphyrins. While most porphyrias will cause high levels of porphyrins in the plasma, increased concentrations in urine and stool are characteristic of PCT. However, urine

tests will fail if the specimen is not protected from light and kept at a high pH. The urine is likely to be reddish or brownish and will glow pink under a fluorescent light. During examination of the urine with a Wood's lamp, characteristic coral pink fluorescence of excessive porphyrins occurs. When a skin biopsy is performed, characteristic changes are seen which differentiates PCT from other blistering diseases. When 24-hour urine and fecal quantitative porphyrin profiles are performed, there are elevated levels of uroporphyrins in the urine and in the stool, coproporphyrins and uroporphyrins.

Other important tests include: Complete blood count to assess hemoglobin levels, measurement of iron stores, which may be increased in over 30% of patients, liver enzymes because the liver sometimes does not function normally, fasting blood sugar because of the increased incidence of diabetes and antinuclear antibodies because of the increased incidence of lupus erythematosus.

The primary treatment is phlebotomy, which involves removing a pint of blood every 1-2 weeks to reduce the amount of iron in the body. Since iron inhibits the deficient enzyme, removing iron via a phlebotomy lowers the porphyrin levels in the liver and plasma. The skin usually becomes normal after five or six phlebotomies. Chloroquine or hydroxychloroquine, which remove excess porphyrins from the liver, can also be prescribed. The PCT patient should also avoid alcohol, iron, estrogens and other factors that cause symptoms. It is important to be careful in the sun and to use appropriate opaque sunscreen and sun protective clothing.

In the US, there is no registry for the porphyrias, so the prevalence of PCT is not known. However, it is estimated at one case in 25,000-50,000 and higher prevalences have been reported in Europe. There are very few people who are homozygous PCT, where both parents have the disorder. Those that are have a very severe form of the disorder known as Hepato-erythropoietic Porphyria (HEP)

**The schedule and instructions to hear the APF Internet Broadcast with Phil Grohs can be found on the APF website.**

## Special Assistance for YOU

We are grateful to Ovation Pharmaceutical, the producers of Panhematin®, for responding to a great need of our members who have the acute porphyrias. They have instituted a special assistance program, the Ovation Reimbursement Support Program, which is a **free** service available to patients, caregivers, medical billing staff, healthcare providers, and others who have questions about insurance coverage and reimbursement-related issues for Panhematin®.

**Billing issues**— Contact the hotline for assistance obtaining appropriate billing codes required on medical claims or if you need additional documentation to submit with your claims.

**Insurance verification**— The hotline representative will contact your insurance company to determine in advance how it will pay for the Ovation product or related procedure in which you are interested.

**Prior authorization support**— The hotline representative can help facilitate the prior authorization process by determining requirements, coordinating paperwork, and following up on the final decision.

**Insurer education**— Representatives who staff the hotline can help educate insurers about Ovation products to expedite coverage and payment.

**Policy monitoring**— The Program monitors public and private pay or coverage policies to ensure you have the most up-to-date coverage information. Representatives will also answer any questions you have about insurance coverage and reimbursement related to Ovation products.

**Coverage appeals**— A hotline representative will review denied claims, explain appeal procedures, make suggestions for resubmissions, and follow-up throughout the appeal process.

**Alternate funding and patient assistance referrals and screening**— The hotline staff can assist you in discovering alternate forms of coverage available to patients and make appropriate referrals, and if necessary, screen patients who have proven financial need for the Ovation Patient Assistance Program.

To speak with a representative, call the toll-free number Monday-Friday, 8-5 EST, **1-866-209-7604** or leave your name and phone number and you will be called within 24 hours. In an emergency, your **physician** can order **Panhematin®: 1-800-706-2191**.

To receive a comprehensive brochure about this new program, please contact the APF office.

## Dr. Peter Tishler

Dr. Peter Tishler who hails from Harvard University, has served on the APF Scientific Advisory Board for over twenty years. He has been instrumental in instigating many of the porphyria patient and physician educational programs.



Along with his clinical and research efforts in the field of porphyria, Dr. Tishler is involved in ongoing studies on the genetics, genomics and natural history of diseases of aging and of physiologic phenomena that change with age. He also is involved in developing the role of genetics in public health, in terms of both improving the health of and educating pop-

ulations. We are proud that our board members, like Dr. Tishler, are experienced in a wide range in the medical field and that they share this expertise in-patient and out-patient consultations for practice for patients with suspect or definite genetic disease, and especially porphyria.

Recently, Dr. Tishler offered to serve as a consultant to review the existing drug lists and help create an expanded version of this compilation of lists, as well as any additional medications that might apply. This is a very comprehensive, time consuming project that cannot be completed without your help. Namely, we are presently conducting a survey in which one of the questions is related to your own experience with safe and unsafe medications. If you have had an attack related to a particular medication, please contact the APF and relate your experience as part of this research project.

## Porphozom Research Complete

**Great News**— The Porphozom research project was completed recently. We want to thank the doctors who worked diligently to conduct the study, our members who participated as patient volunteers and Zymenex, the company that has prepared Porphozom, the enzyme replacement being studied.

The next step in the process is to assess the results of the research. We will report these results to our members as soon as we have information. It is our hope that this treatment will profoundly improve the health of those people who are suffering an acute attack.

## Reaching Goals for National Porphyria Awareness Week

In January, we mailed to you a letter for the National Porphyria Awareness Week (NPAW) February 18-25. We hope that this letter encouraged you to reach out to others in your community so that they may become aware of porphyria. The goals of the American Porphyria Foundation are to enhance public awareness, increase educational opportunities and support research.



Specific NPAW goals were to create a stronger broad based knowledge of the disease through our members, foundation and the media, as well as to reach out on a grass roots level to members' communities. Media attention has been a success! Parade, National Geographic, CNN's Anderson Cooper 360, episodes of award winning television shows "House" and "Scrubs" have aired. One of our members, Phil Grohs, even has dedicated time to his Internet radio broadcast to cover porphyria related stories.

We still need your help to broaden the In Touch outreach program by hosting an In Touch meeting in your state. These meetings enable you to meet other members with porphyria, share advice, build camaraderie, and receive unique peer-to-peer emotional support not easily found anywhere else. Our In Touch coordinator is Lelia Brougher, and she'll be happy to help if you are interested in joining the In Touch network or even hosting an In Touch meeting. Lelia can be reached at 404-550-4880. Remember, there is no charge to be in this helpful program, if you are a foundation member.

We thank those who have been helping to make NPAW a success, and we will share their stories in a later newsletter.

## You Can Own a Piece of History

One of our members recently purchased an handwritten original letter by King George III. It is now known through DNA studies that King George definitely had porphyria. Some historians believe that his illness so impacted the English rule of the Colonies that they lost the Revolutionary War. King George writes about his illness in this letter.

Our member has allowed us to make superb copies that are antique in appearance and are suitable for framing. Included in this package are also the transcription of the letter, as well as a history of George III and how it relates to porphyria. All of this can be sent to you in a beautifully bound folder for only \$50 donation to the APF.



## With In Touch, You Are Never Alone!

Don't miss out on one of the greatest benefits of being an APF Member! Please JOIN our IN TOUCH network along with hundreds of others. This network enables you to meet others with porphyria through email, meetings or other forms of contact. Who knows, someone with porphyria could be in your hometown. There is no charge to be in this helpful program if you are a foundation member. We only require that you sign a permission slip authorizing us to release your name and contact information. Our members' privacy is of utmost importance to us. It's simple to join — print out the permission slip under the IN TOUCH link on our website or contact us directly, and we'll be happy to provide you with a copy to sign.

The IN TOUCH network is a helpful and highly motivated group of APF members who are available to offer support to others. Members of the network list their names and their preferred contact information only to other APF members. From there, members communicate with one another, share advice, and receive unique peer-to-peer emotional support not easily found anywhere else.

We are now beginning to schedule our IN TOUCH meetings. These meetings provide you the opportunity to meet other members in your area. Plus, we usually have a porphyria specialist make a presentation and answer questions on a phone hook up during the event. If you would like to host an IN TOUCH meeting or join the IN TOUCH network, please contact our coordinator, Lelia Brougher, who can be reached at [email@broughers.com](mailto:email@broughers.com), or 404-550-4880.

**ENEWS—** To receive the frequent E-News Updates, email [Elizabethapf@aol.com](mailto:Elizabethapf@aol.com) with your email address. Please make sure to let us know if you make an email address change.

## Autosomal Dominant A Family Dilemma

Autosomal Dominant. That word quickly became a burning icon within me after I was diagnosed with Acute Intermittent Porphyrria in 1996. Sure, there was a period of shock for myself as that diagnosis only added more pain and distress to my cervical spine injury, which had already resulted in my disability. Dr. Paul LeCat, who is now with the Akron General Hospital in Akron, Ohio, sat with me and explained AIP and how it would affect me and how it could affect my children. (I have since characterized he good doctor as “more than a doctor, but a true healer.”)

An autosomal dominant gene carries a defect that can be passed on to the children of the afflicted parent. Each child has a 50% chance of inheriting the illness. That’s not to say if you have four kids that two of them will be sick. It’s a flip of the coin for each one. All four could be so afflicted, none could be afflicted or the truth would be somewhere in between. Sure I was worried about myself because I was really sick, but I was more concerned about my kids.

Well, here we are 10 years later at a family reunion. The Porph Monster has not showed itself in any of my three sons yet. As a family, we’ve taken the approach “If It Ain’t Broke, Don’t Fix It!” My advice to my sons has been not to worry and go live a happy life, but if they find themselves sick or injured, they should always include in their medical history that their father has AIP, an autosomal dominant disease.



In the photo from left to right: John is 37 and General Manager of a new car auto dealership in upstate New York. He’s married to Tisha, and they have a beautiful daughter, Lily. Steve, our youngest, is 27 and is a restaurateur in northeastern Florida. Margaret is the lady who taught us all how to be true gentlemen. Then there’s me, *Jack Finnegan*.

Next is Brian who is 34 years young and is a real estate developer in central California and his partner, Bruce Kahl.

There you have it. Could it be that we’ve flipped heads three times in a row and none of our sons have AIP? Possibly, only time will tell. But for now we’re happy, successful and together. That’s the way it should be.

**Editor’s note:** We would like to have your story as well. Please send it to [lyonapf@aol.com](mailto:lyonapf@aol.com) or write it and send it to the APF office.



## Protect the Future Exciting News

**We have reached our goal for year one!** As most of you know, there is a real concern about training porphyria experts for the future?

Since these issues were important to each of us, we began a campaign to identify and train new experts. We recently reached our goal for Year One and are in the process of identifying a doctor to train as a specialist. He or she will then be engage in the intensive training required to be a porphyria specialist.

Watch for the announcement of the “Protect our Future” Award Winner!

## Take the Survey

Because many of you have had difficulties with porphyria diagnosis and treatment, as well as problems securing insurance coverage and insurance claims, we are seeking to determine how best to help with these problems by asking you a few important questions. Our goal is also to enhance our patient and physician education programs.

Therefore, over the next few months, you will be contacted by one of our APF staff to complete a survey to help secure information on the above issues. We would appreciate your help to complete these surveys timely. You may also receive the survey via email. If so, we would appreciate your taking the survey that way. If you would like to elaborate on a question, please call Desiree at the office.

Thank you in advance.

## EPP Primary Care Physician/ Emergency Room Kits Ready



The EPP Primary Care Physician and Emergency Room Kits are ready. They are filled with useful information for you, your family, your doctor and other medical professionals, especially in the Emergency Room. In addition, you will find brochures, fact sheets and even a sample of Total Block, one of the best sunscreens on the market. Contact the APF to purchase the kit for only \$25. The price on the EPP kit and the Acute Porphyria kit has increased

as the information is more costly than the previous cost of the kit. If you do not have a kit for the acute porphyrias, you really should purchase one. They are so useful, comprehensive and extraordinary that they are now being copied by other organizations.

## \$\$\$\$\$ Matching Grant \$\$\$\$\$

**Never before will your gifts to the APF go such a very long way.**

To help the APF expand our educational programs, an APF member has graciously offered to match your donations dollar for dollar up to \$ 15,000. This includes your donations when you join the APF or renew your membership. We have never had such a generous opportunity and are most grateful. We ask that you, too, take advantage of this most charitable offer and send your gift today in the enclosed envelope.

**Editor's Note:** *Recently, I got an email that said, "You are all about fundraising." That made me sad, so I replied that the APF was our foundation, not mine or the office staff. And that we were working together to try to help enhance awareness and educate patients and physicians about porphyria and that takes money. Together we have done an amazing job. Let's keep it up.*



*The information contained on the American Porphyria Foundation (APF) web site or in the APF newsletter is provided for your general information only.*

*The APF does not give medical advice or engage in the practice of medicine. The APF under no circumstances recommends particular treatments for specific individuals, and in all cases recommends that you consult your physician or local treatment center before pursuing any course of treatment.*

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## What's New on the APF

**Don't forget there are new additions on the APF website: [www.porphyrifoundation.com](http://www.porphyrifoundation.com)**

**It is time to schedule the IN TOUCH meetings for 2006.** If you would like to host a meeting, please contact Lelia Brougher, our IN TOUCH coordinator, at the APF office or call her at 404-550-4880. It's time to get IN TOUCH!

**Buy the new EPP kit** or the Primary Care/ER Kit for the Acute Porphyrias, the *Porphyria Live* DVD, the book *Porphyria, A Lyon's Share of Trouble* for \$25 each. Contact the APF or purchase the items over the website.

**Instructions are on the website to hear the APF intern broadcast with Phil Grohs.**

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