# ANTIPHOSPHO...WHAT?

APS Foundation of America, Inc. Newsletter

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## INR Monitoring in Patients with Antiphospholipid Antibodies with Finger Stick INR Devices

**Written by: Stephan Moll, MD**

A superb way to monitor INRs (International Normalized Ratio) in patients on oral anticoagulants who do NOT have antiphospholipid antibodies (APLA) is though use of "point of care instruments", where the INR is tested on blood from a finger stick [1]. This method gives fast results and is used by many physicians' offices and by some patients at home. However, in patients with APLA on oral anticoagulants these instruments may give inaccurate readings [1,2].

**"In one third of patients with APLA the INRs read by these point of care instruments are unreliable..."**

In one third of patients with APLA the INRs read by these point of care instruments are unreliable: (a) they either give INR values that are too high, compared to INRs tested in a laboratory from an intravenous (i.v.) stick [2], or (b) the instruments flash up an error message [3]. This inaccuracy is likely caused by the presence of the APLA. Since antibody levels can fluctuate over time, the instrument may give accurate readings at times when the antibody levels are low, but inaccurate ones at times when the levels are higher. This is a phenomenon not unique for one particular instrument, but is seen with the Coaguchek®, INRatio® and ProTime® instruments [2,3].

Because of the potential inaccuracies of these point of care instruments in patients with APLA, it is preferable not to use them for INR monitoring in APLA patients. Instead, oral anticoagulant monitoring should be done from i.v. blood draws through a laboratory. However, if a health care provider or a patient with APLA decide to use an INR point of care monitor for oral anticoagulant management, it is appropriate that the reliability of the INRs obtained with the instrument be determined. This can be done by simultaneously obtaining an INR from a finger stick and the point of care instrument, and also from an i.v. stick and a laboratory method. This comparison should be done when the instrument is first used, and then every so often thereafter, such as every 6 months. If the machine gives unreliable readings, the patient should be switched to i.v. stick INR monitoring via a laboratory. Alternatively, one could correlate the INRs obtained with the INR point of care machine to the laboratory INR, and, thus, determine a patient's unique therapeutic range with the machine. However, this is a cumbersome process.

Finally, it is important to keep in mind that some patients with APLA who are on oral anticoagulants have an invalid INR even with an i.v. stick and laboratory determined method [4]. Alternative tests, uninfluenced by the lupus anticoagulant, need to be used for oral anticoagulant monitoring. Tests that could be used are factor II activity, chromogenic factor X, or Prothrombin-proconvertin time [4].


***References:***

1. Moll S, Wobbleton DL, Misita CP, Bryant B, Malone R, Musty M: INR Determination by plasma-based methods versus point-of-care instruments in patients with antiphospholipid antibody syndrome on anticoagulants. Int Soc Thromb Haemost meeting; Sydney, Australia, Aug 2005. *J Thromb Haemost*. 2005 Aug;3(suppl 1);abstract.
2. Perry SL, Samsa GP, Ortel TL: Point-of-care testing of the international normalized ratio in patients with antiphospholipid antibodies. *Thromb Haemost* 2005 Dec;94(6):1196-202.
3. Yang DT, Robetorye RS, Rodgers GM: Home prothrombin time monitoring: a literature analysis. *Am J Hematol* 2004;77:177-186.
4. Moll S, Ortel TL. Monitoring Warfarin Therapy in Patients with Lupus Anticoagulants. *Ann Intern Med* 1997;127:177-185.



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*This article is adapted from Q/As published by Dr. Moll at www.fvleiden.org/ask/94.html and www.fvleiden.org/ask/56.html*

*"It is so much easier to cope with this disease when you have others dealing with the same to talk to cry to and even let out our anger with." APS Friends & Support Forum Member, Virginia, USA*

## Friends of APSFA

Do you believe in our cause? If you do, you can now become a "Friend of APSFA". For a fee of $25.00 you will get our Friendship package which includes:

- Our quarterly newsletter in paper form
- 1 year 'sample' Anticoagulation log book
- Printed copy of all our Brochures
- APS Awareness pin

If you would like to become a "Friend of APSFA" please visit our website for how to do so. More information is located at www.apsfa.org/friends.htm.

## We Need Your Help!

We are in *need* of patient stories and Newsletter articles. If you would like to contribute something, please email us at articles@apsfa.org

We are also searching for doctors who are currently treating APS patients for our Dr. List. Please see our website for more details.

**Inside this issue:**

## Letter from the President

*In June, we turn 2 years old. I am sure there are many that thought we would never make it that far. The APSFA has a team of hard working, dedicated volunteers and medical advisors helping to make it happen. Thank You for all that you have done!*

*The past two months have been quite busy for the APSFA. We have attended or been represented at Grand Rounds at Ohio State University, seminars in MI, PA (both for the professional and layperson), MN, IL, NM, a Lupus Conference in KS and a MS Walk in VA. We reached at least 3,500 people face to face. Not to shabby for two months.*

*The APSFA has declared June as APS Awareness month and is sending petitions to several states to make June APS Awareness Month. We will be attending conferences, medical seminars, grand rounds and health fairs to share the patient perspective and provide awareness of APS throughout the month of June and also encouraging the community to "Get in the Flow". Individual and APSFA fundraisers will be occurring throughout the country to help promote APS Awareness and help support the mission.*

*Please keep an eye for our Press Releases! If you would like to make sure your local media picks them up, please email us and we can get them to you to send out. If you would like to ensure your state makes recognition of this and would like to request a proclamation from your governor, drop us an email and we will help you with that as well.*

*2006 as a whole proved to be a pretty good year for a first full year. Here are some of the quick highlights: the APSFA home page benefited 34,896 people, TV show aired on National TV, Made Press in 5 different media venues that we are aware of, and we attended Grand Rounds & other seminars that benefited about 500 people. As you can see we have we are moving ahead in 2007 by leaps and bounds. For the full year end report, please email the APSFA at apsfa@apsfa.org.*

*Our support forum is also growing by leaps and bounds. We are over 1,250 participants strong and have an average of 2,298 posts per month! It really is a very active support forum. We are proud to be able to offer the level of support and information that we do.*

*Once again, I hope this newsletter finds you in the best of health and with a perfect INR level.*

*Sincerely,*

*Tina Pohlman*
*President & Founder*

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# MO-KAN Spreads APS Awareness

**Written by: Dana Stuart**

"Mo-Kan" is a phrase commonly used in the Missouri-Kansas region to describe various missions or goals that Missouri and Kansas businesses and residents CAN accomplish together. Frequently used for public service announcements, advertisements, and other miscellaneous uses, "Mo-Kan" has become the unofficial slogan for several alliances, which have formed for some very worthy causes. Now "Mo-Kan" spreads APS Awareness!

On May 5, 2007, I had the privilege of representing the APS Foundation of America, Inc. at the Lupus Foundation of America's Kansas City Chapter Conference, which is held annually and open to Missouri and Kansas, patients and families, in the KC Metro Region, which covers Missouri and Kansas. The KC Lupus Chapter did an excellent job planning and executing this conference and much of the information obtained from this conference was applicable to APS patients. There were approximately 200 patients in attendance. Break-out sessions included patient oriented topics such as coping with migraine headaches, controlling blood pressure, and even a workshop to instruct patients on how to test for protein in the urine. Dr. Nabih Abdou, a rheumatologist from St. Luke's Hospital, dedicated a portion of his lecture to Antiphospholipid Antibody Syndrome and promoted the APS Foundation of America, Inc., which we greatly appreciate. I was allowed to distribute a large amount of APSFA literature to patients and families, which we can't thank the Lupus Foundation enough for.

I also had the distinct pleasure of meeting with Missouri Governor Matthew Blunt on March 14th for a ceremony to proclaim the month of June, "APS Awareness Month." During this ceremony, I was able to share information about APS and about my twins who were born premature and passed away on November 17, 2005.

Sometimes it seems that we have so far to go to raise the level of awareness that APS patients need to receive adequate treatment. On the other hand, it's hard to believe with the progress we are making, that we have only been in existence for two years. I am just one individual and look what I was able do to. You can do this too!

# June is APS Awareness Month: Get in the Flow!

Antiphospholipid Antibody Syndrome Awareness
APS Foundation of America, Inc. www.apsfa.org

The APS Foundation of America, Inc. (APSFA) has declared June as National Antiphospholipid Antibody (APS) Awareness Month. We are educating the public and medical community about this disorder, urging people to Get in the Flow!

This disorder threatens to become more common than Lupus and Multiple Sclerosis.

The APSFA is sending petitions to several states to make June APS Awareness Month. The APSFA will be attending conferences, medical seminars, grand rounds and health fairs to share the patient perspective and provide awareness of APS throughout the month of June and also encouraging the community to Get in the Flow. Individual and APSFA fundraisers will be occurring throughout the country to help promote APS awareness and help support the mission.

Knowing more about APS can make all the difference. Get in the know and Get in the Flow!

# APS in the Community

**Written by: Seren Estrada**

March of Dimes
Saving babies, together

On April 22nd the APSFA made an appearance at the annual March of Dimes WalkAmerica event in Springfield, Virginia. Informative brochures and booklets were made available to hundreds of preeclamptic mothers and those who suffered from tragic fetal loss. This sparked enough interest that the materials were requested at the National March of Dimes WalkAmerica event in Washington D.C. the following weekend! Thousands of mothers, fathers and others who have been touched by a pregnancy gone-wrong were exposed to critical information about APS. The national chapter of March of Dimes in DC currently brings the materials when they are out in the public.

## Father/Daughter APS Patient Story ~ Sylvia

**Written by: Sylvia from Arcadia, FL USA**

Hello, my name is Sylvia. I'm 16 years old, and I have an autoimmune disease called Antiphospholipid Antibody Syndrome (APS). I was diagnosed with it after my dad suffered his first DVT. They tested him for it because there wasn't a reason why an active young man such as my father should develop a blood clot. After his problems started getting worse, we decided that my brother and I should get tested as well. The doctor didn't want to test us as he said the chance of us having it was very low. My brother came back negative but I tested positive.

My dad had just turned 38 when he passed away on December 21, 2006 from long years of struggling with APS. Upon his final trip to the hospital, they diagnosed him with Catastrophic Antiphospholipid Antibody Syndrome (CAPS). I just have this feeling that if he could have found a doctor that was APS literate, it wouldn't have claimed his life so quickly. It took months after his first DVT to find a doctor who had even heard of APS, and by that time his DVT was just plaque embedded in his vein.

During the past 4 years, my dad endured many hospital stays and surgeries. He had 7 DVTs – 3 in his arms and 4 in his leg. 2 arterial clots – 1st they did a thrombectomy, and then a year later they took a vein out of his left leg and made it into an artery in his right (that surgery only lasted a couple months). After putting the Vena Filter in, he had 3 heart attacks and an angioplasty.

He was on several different medications for many different reasons. He started out with Coumadin and found out he was resistant to it. No matter how high of a dose his INR never changed. They started him on Lovenox injections for a couple of years and even that stopped working. Then they then found a new medicine, Fragmin. The recommended dose is 10,000 units once a day....he was on that 3 times a day.

In his last months, he was forming clots all over his body and lungs and the doctors couldn't explain why. They did test after test and called specialist after specialist, but just couldn't prevent the clots. His liver started shutting down and his body became weaker. The doctors told us that there was nothing else they could do, and they sent him home with Hospice.

I have a lot of the same symptoms my dad did, such as headaches, dizzy spells, brain fog, blotchy patches, tightness, and tingling of the arms. But then again, I have some symptoms he didn't experience, such as bad menstrual cycles.

Right now I'm seeing a pediatric hematologist, but it doesn't seem like she is taking my symptoms seriously. My mom has a copy of my medical records and is sending them out to different doctors to see if one of them knows about APS and will be willing to treat me. I believe that prevention is the best way to fight this disease, and that is what I'm attempting to do.

## Tips for Preventing Heat-Related Illness

**Submitted by: Tina Pohlman**

The best defense is prevention. Here are some prevention tips:

- Drink more fluids (nonalcoholic), regardless of your activity level. Don't wait until you're thirsty to drink. Warning: If your doctor generally limits the amount of fluid you drink or has you on water pills, ask him how much you should drink while the weather is hot.
- Don't drink liquids that contain alcohol or large amounts of sugar–these actually cause you to lose more body fluid. Also, avoid very cold drinks, because they can cause stomach cramps.
- Stay indoors and, if at all possible, stay in an air-conditioned place. If your home does not have air conditioning, go to the shopping mall or public library–even a few hours spent in air conditioning can help your body stay cooler when you go back into the heat. Call your local health department to see if there are any heat-relief shelters in your area.
- Electric fans may provide comfort, but when the temperature is in the high 90s, fans will not prevent heat-related illness. Taking a cool shower or bath, or moving to an air-conditioned place is a much better way to cool off.

- Wear lightweight, light-colored, loose-fitting clothing.
- NEVER leave anyone in a closed, parked vehicle.

Although any one at any time can suffer from heat-related illness, some people are at greater risk than others. Check regularly on:

- Infants and young children
- People aged 65 or older
- People who have a mental illness
- Those who are physically ill, especially with heart disease or high blood pressure

Visit adults at risk at least twice a day and closely watch them for signs of heat exhaustion or heat stroke. Infants and young children, of course, need much more frequent watching.

If you must be out in the heat:

- Limit your outdoor activity to morning and evening hours.
- Cut down on exercise. If you must exercise, drink two to four glasses of cool, nonalcoholic fluids each hour. A sports beverage can replace the salt and minerals you lose in sweat. Warning: If you are on a low-salt diet, talk with your doctor before drinking a sports beverage. Remember the warning in the first "tip" (above), too.
- Try to rest often in shady areas.
- Protect yourself from the sun by wearing a wide-brimmed hat (also keeps you cooler) and sunglasses and by putting on sunscreen of SPF 15 or higher (the most effective products say "broad spectrum" or "UVA/UVB protection" on their labels).

This information provided by NCEH's Health Studies Branch: http://www.bt.cdc.gov/disasters/extremeheat/heattips.asp

# Thrombosis Education Days ~ MI & Chicago

**Written by: Heidi Ponagai**

**Dr. Moll with Todd and Heidi**

The National Alliance of Thrombosis and Thrombophilia (NATT) and the MSU Center for Bleeding and Clotting Disorders held an education day on March 24th in Lansing, Michigan for people who have had blood clots, who have clotting disorders, and their families and friends. We were fortunate enough to get a booth at the seminar to display and distribute APSFA brochures and booklets to people.

First let me say that if you have an opportunity to attend something like this, please try to make it there! This seminar was very good, informative, and a great chance to get to ask specialists in the field some questions you may have. You will also meet other people with similar problems in your area, and how comforting is it to know that you are not alone? It was really an eye opening experience for me. I don't know what it's like to live after having a blood clot and they had a couple of really good patients who told their stories. I also learned a lot from the lecture portion of the seminar. I never quite understood how clots were formed or what the difference between the clotting disorders is and due to the excellent slides and speakers, I learned the difference.

My husband, Todd, who has APS, and I were in touch with Dr. Stephan Moll from NATT prior to the seminar. Dr. Moll asked me to send him Todd's photo and story so he could talk about Todd in his lecture. It was great to see Todd's picture up there and kind of funny to hear about Todd's symptoms and syndromes in a lecture like that. Dr. Moll referred to Todd's situation quite a bit and also said a few things about the APSFA.

In between the doctors speaking, there was a very inspirational personal story from a woman who is from Michigan, has FVL and has had two DVT's; one in each arm. She ate the right foods, was healthy, exercised, etc. and now she can barely do anything because of the risk of her forming another clot in her arms. She had to give up many things she really loved to do like playing the piano and swimming. She really broke down what it's like to have gone from a healthy individual to having a clot, and her speech really opened my eyes. The entire seminar was captured on video and will eventually put it on a website. When it is, we will be sure to share it with our forum and on our blogs. Her segment is a MUST see, especially for family members and caregivers of people who have had clots. I had tears in my eyes. It was excellent.

At lunch, we ate with the people who helped organize the event because we were technically a "vendor". It was very nice to talk to the ladies in charge about the foundation and we were able to share our feedback on the event. The APSFA will definitely be invited again if this becomes an annual event. We also had an interesting conversation with a woman who was there representing a home INR machine company. Upon us asking, she was very honest with us and said that INR machines do not work for APS patients. I thanked her profusely for validating what we have been trying to tell people for a long time!

The main topics of the MI seminar were: blood clots – description, treatment, preventative measures, and who is at risk, clotting disorders and the differences between them, inherited clotting disorders, women's health issues as far as clotting is concerned, and pediatrics blood clots.

The speakers were: Dr. John Penner, Professor for the MSU Department of Medicine & Director of the Adult MSU Center for Bleeding and Clotting disorders, Dr. Roshni Kulkarni, Director of the Division of Blood Disorders for the CDC & Professor at the MSU Department of Pediatrics, Dr. Stephan Moll, Director of the UNC at Chapel Hill Thrombophilia Department and the Chair of the Medical and Scientific Advisory Board for NATT, Susan Mohr, FVL patient and blood clot survivor from Michigan, Dr. Ajovi Scott-Emaukpor, Professor for the MSU Dept of Pediatrics and Director of the Pediatric MSU Center for Bleeding and Clotting Disorders, Dr. Renuka Gera, a professor for the MSU Department of Pediatrics and the Associate Chair for Pediatrics, Karen Boyd, MSU Center for Bleeding and Clotting Disorders, and Kathy Reed, NATT.

Todd also attended another similar seminar on May 5th in Chicago sponsored by NATT. He was asked by Liz Vargas of NATT to attend the luncheon that was held between the professional and patient parts of the seminar. Todd was able to network with the doctors and other speakers during the luncheon.

In between the luncheon and the patient seminar, Todd handed out APSFA materials and business cards. We were not able to get a table at this seminar, but Todd brought a backpack full of our materials to give to people. Todd also took this opportunity to speak to the numerous home INR machine companies that had booths set up. He asked the representatives whether the INR machines are safe for APS patients and then shared the very negative experience that he has had with the machine with them. Some of the representatives were shocked to hear of such a problem and some were aware of the problems between APS patients and home testing.

When the patient seminar started, Dr. Moll, who was also speaking at this seminar, asked Todd to sit close to the front so he could refer to him again during his lecture. During the Q & A section of the afternoon, Todd was given a chance to talk a bit about his bad experience with INR testing with a Hemosense INR machine in the clinic. He was also given the opportunity to talk a little bit about the foundation.

Again, I'd like to stress that if a similar seminar or education day is held in your area that you make an effort to attend. You will not walk away without learning something and you will have an opportunity to ask questions to specialists in the field. Bring along a friend or family member and they will be educated too!

In a matter of two afternoons, Todd and I were able to reach out to approximately 300 people, which is an excellent feat for the APSFA! We're really getting our name out there and showing people what we're all about. We hope that one day in the future, APS and the APSFA will be a household name!

# Hydroxychloroquine – Everything Old is New Again!

**Written by: Gale McCarty, MD, FACP, FACR**

### What is Hydroxychloroquine?

Hydroxychloroquine (HCQ, or its trade name-Plaquenil) has a long and honored history of use in systemic lupus erythematosus (SLE) as a general medication to decrease activity of the immune system and decrease symptoms. For years it has been approved for use by the FDA for lupus and rheumatoid arthritis, and has been used most frequently for skin and joint manifestations. It is considered a mainstay of therapy for any patient with SLE by many lupus experts and rheumatologists. It has many mechanisms of action, some related to decrease in the activity of the immune system, and some related to effects on blood clotting mechanisms. HCQ belongs to the class of drugs call anti-malarials, which includes Chloroquine and Atabrine. (This does not mean that anyone thinks that SLE or APS is caused by the agent that causes malaria-like most discoveries in medicine, it was the chance observation that patients with some autoimmune diseases who got anti-malarial drugs to prevent malaria when traveling to likely areas of infection noted their symptoms improved on HCQ). One of the most complete and excellent reviews of all the literature on the anti-malarials to which all patients and their physicians are directed is Dr. Dan Wallace's Chapter 59 in the Wallace-Hahn Dubois' *Lupus Erythematosus* textbook. Another excellent review on APS therapy in general has been published by Dr. Robert Roubey.

**"...HCQ did act as an anticoagulant."**

### From SLE to APS-How HCQ Came to Be Used-A Brief History.

Research in medicine involves taking a concept as far as one can with the technology at hand, and then years later it is "*re*-searched"-someone rediscovers a concept and extends it with new technology or a fresh approach to test a hypothesis. Orthopedic surgeons Dr. Carter and his colleagues were looking for an alternative to heparin to prevent blood clots after various orthopedic surgeries. They discovered that HCQ acted as an anticoagulant in these patients who did not have SLE or APS. When patients were asked to take it several days before surgery, and a few days after, they did not suffer from blood clots after surgery, much as if they had been given heparin. However, using HCQ to prevent blood clots in SLE or APS patients did not become part of mainstream rheumatology at this time.

Dr. Michelle Petri first noted in the Hopkins Lupus Cohort that lupus patients on HCQ who had antiphospholipid antibodies (aPLs) seemed to be protected against having the usual consequences of aPLs-thromboses or blood clots. Along with other factors acting on blood vessels, aPLs were shown to be independent predictors of blood clots. This was a "looking-back" or retrospective study.

Dr. Sylvia Pierangeli in the laboratory of Dr. E. Nigel Harris made blood clots in mice by making a "pinch" injury in a blood vessel, then looked at the mechanics of blood clots formed in those vessels when patient aPL antibodies were injected. Their model was a major advance in the field of "APSology". In '97, Dr Edwards in their lab found that when HCQ was added to the injured mouse blood vessels when patient aPLs were around in the mouse model, HCQ did act as an anticoagulant. Showing that HCQ had these actions was very important in showing that what previous physician-investigators saw-protection from blood clots in patients with SLE and APS-could be reproduced in a mouse model of APS.

### Taking Lessons from the Literature Into the Clinical Setting.

*I felt this data could logically be extended to using HCQ for patients with APS with and without SLE in a "looking-forward" or prospective study, and we began treating patients this way, staring with the Indiana APS Database Cohort in '96.* In my academic rheumatology clinics, I have been using HCQ 200mg by mouth one tablet twice a day, and one baby aspirin 81mg once a day (low dose ASA or LDA) in APS patients with and without SLE. How HCQ is distributed in individual patients and what levels are maintained in patients has not been well studied directly. It is known that smoking can decrease HCQ action, and overweight patients might require higher doses for efficacy. Checking blood HCQ levels, as some medications are in autoimmune diseases, is not generally considered necessary (see later comments).

As HCQ takes several weeks to work in most diseases, and stays around for several months after it is stopped, some of its anti-inflammatory effects can be seen in individual patients as early as 2-3 weeks, but usually reach a maximum efficacy at approximately 3 months. Interestingly, in our 3 academic rheum unit cohorts, the time that it took for patient aPL levels to respond by showing a decrease in aPL levels was remarkably consistent (Table 1). As we had an ethical concern not to deny the use of HCQ to APS patients with and without SLE in our prospective study, we did not use the time-honored "placebo (sugar pill)" to create a control group.

Table 1. TIME COURSE OF aPL CHANGES ON HCQ RX

| Cohort: | MEAN MONTHS TO DECREASE +/-sd: | MEAN MONTHS TO NEGATIVE +/-sd: |
|---|---|---|
| 1 | 3.17 +/- 0.96 | 5.10 +/- 0.27 |
| 2 | 3.56 +/- 0.95 | 5.80 +/- 0.56 |
| 3 | 3.41 +/- 0.89 | 6.16 +/- 0.61 |

Cohorts 1 and 2 were followed for 4 years, and Cohort 3 for 2.5 yrs. These APS patients were not significantly different across the centers: 91% were female, 80% white, 63% had APS without SLE. The patients met the Sapporo Criteria for diagnosis (see my prior Newsletter articles for Sapporo Criteria discussion and references). Their mean age was 39.8 +/- 1.22 yrs.

The APS-related features were: arterial thromboses in 68.1%, venous thromboses in 31.7% , recurrent fetal loss in 23.4%, thrombocytopenia in 42%, livedo reticularis 70.5%. Their aPL/LAC profiles were: IgG anticardiolipin 60.2%, IgM anticardiolipin 32.3%, IgA anticardiolipin 11%, aPTT 28.8%, DRVVT 13.7%, anti-phosphatidylethanolamine 59%, and anti-b2gp1 9%.

### A Closer Look At The Data Using A Different Method of Analysis.

We decided to analyze two outcomes: 128 of the patients had the number of months to aPL level decrease evaluated, and 126 had the number of months to aPL levels becoming negative evaluated. The method we used was called recursive partitioning where the data was sampled and re-sampled by a statistical software program that looked for IF/THEN decision points or decision rules. We wanted to identify factors that affected the months to decrease or the months to negative for all patients related to age, race, and whether they had SLE or APS.

Overall, the mean months to see aPLs decrease was 3.34 months; the mean months to see aPLs negative was 6.63 months.

*article con't on page 8*

# Living with APS: An Autoimmune Disease

**Poem Written by: Nancy Pilonieta**

*Living with an autoimmune disease in not easy*
*People look at me and think you don't look ill*
*But they have no idea how bad I can sometimes feel*

*My legs feel heavy and sometimes I walk with pain*
*At night, my legs keep me tossing and turning*
*My life has not been the same*
*Out of nowhere the headaches hit me*
*And at times my vision becomes blurred and with wavy lines which can make it hard to see*
*I can't do the same amount of activity*
*No more dancing, or long walks for me*
*They wear me out to the point of fatigue*
*I get confused and forget things easily*

*Stress is my enemy*
*It makes my symptoms go crazy*
*Many say think positive*
*That is easy for them to say since they are not I*
*Their lives are not affected to the same degree*
*By a disease whose horrible affects that from the outside can be hard to see*
*For my disease does the most damage inside my body*
*The pain, swelling, and heaviness of the legs*
*The fatigue and how irritated it can make me*
*These things come and go*
*And I never know for how long they will be*
*So I take my pills and see my doctor regularly*
*But what a pain my APS can be*

*When I had blood clots in my legs and lungs*
*I thought "God is this the end of me?"*
*He decided my work on earth was not done*
*But it is scary when new symptoms come*
*For the same question comes to mind*
*Will the end come sooner for me when I feel ill?*
*I leave it in God's hands, as I should do*
*But I have to be honest and say that I worry still*
*For I know my life will never be as it was before APS attacked me*
*And for loved ones this fact can be hard to face*
*Since they look at me and see someone who from the outside is healthy*
*But as I said before they don't see the struggle when APS hits me badly*

*I fight a day-to-day struggle with my disease*
*But I promise those that love me to try and be happy*
*I will have my ups and downs*
*I will adjust to this new life*
*A life with an autoimmune disease*

# Are Natural Alternatives to Warfarin Safe and Effective?

**Written by: Randy Rauber, Pharm.D Candidate**
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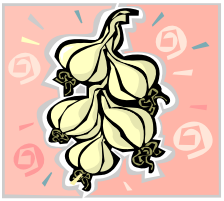

Is there any evidence to support the use of herbal supplement "blood thinners" in patients with antiphospholipid antibody syndrome (APS) as natural alternatives to Warfarin? There are many herbal supplements that claim to be "blood thinners" and appear to have anticoagulant activity: garlic, ginger, ginkgo, dong quai, Feverfew, fish oil, vitamin E, etc. Most of these products work by inhibiting platelet aggregation and activation, which is similar to the way aspirin works. Theoretically, these agents could be useful in preventing arterial clots. These clots can be a problem for people with APS. Warfarin is not very effective in preventing arterial clots.

The clinical trial data is poor in prevention of clot formation with herbal supplements making it difficult to identify their efficacy and safety. The data provided for these herbal supplements, whether it is how it works or possible indications are mostly performed on animal models. Animal studies never prove safety or effectiveness in humans. It is important to understand that herbal supplements are currently not regulated by the FDA or other government bodies or organizations. In contrast to prescription medications, there is no assurance that herbal products are standardized regarding contents, purity, or safety and efficacy. This means that, unlike prescriptions medications, there is no assurance that the amount of herb contained in the bottle, or even dose to dose, bottle to bottle, are the same as what is stated on the label.

Currently, Warfarin appears to be the best treatment option for APS patients that have had a previous clot, but due to the unique mechanism of the disease it is not deemed as the perfect solution to preventing clot formation. A study published in the Journal of American Medical Association found that only 1% of all patients who have APS develop a clot, but the risk increases to 10% for those with a prior clot. Warfarin therapy has demonstrated a decrease of 80 to 90% in recurrent venous thrombosis for this patient population. In contrast, aspirin has a role in patients with APS as a preventative treatment for patients that have not had a clot. It is unknown if herbal supplements will find a role in the treatment of clotting of patients with APS.

I don't think these medications should be used in this type of therapy until clinical data is provided proving the efficacy and safety for the indication in prevention of blood clots. One bit of caution – you should be very cautious of people who make vague claims of effectiveness for any product when the person making the claim will profit if you purchase the product.

*Hydroxychloroquine ... continued from pg 6*

**For the patients with months to decrease of aPLs as the outcome**, the decision points were **race, age, and having APS alone** (what was called primary APS or APS without SLE).

IF the patient was white, was <56.6 yrs old, and had APS without SLE, THEN the patient had the fastest response to HCQ in terms of the aPLs decreasing (2.84 months).
IF the patient was black, was >56.6 hrs old, THEN the patient had a slower response to HCQ in terms of the aPLs decreasing (3.87 months).

**For the patients with months to negative aPLs as the outcome**, the decision points were **age and race**.

IF the patient was <54.5 yrs old, THEN it took 6.91 months for aPLs to disappear.
IF the patient was >54.5 yrs. , THEN it took 8.90 months for aPLs to disappear.
IF the patient was white, THEN it took 5.84 months for aPLs to disappear.
IF the patient was black, THEN it took 8.19 months for aPLs to disappear.

Efficacy of LDA and HCQ treatment in aPL reduction is affected by age, race, and APS type.

Our prior data in one of the 3 cohorts where it was systematically studied has shown a relationship of age vs. body surface area to rates of aPL decrements. This likely reflects how individual patients process HCQ once in the body, or to other aspects related to drug metabolism as reflected by age and body weight. As most of the patients were on prescription generic HCQ, as opposed to a brand name HCQ, it is not likely a difference in the drug formulation. As we did not look at HCQ levels in our studies we can't fully answer this question.

Additionally, we noted several other areas of improvement consistent with the time course of HCQ action in our patients:

a) the frequency and severity of migraines decreased
b) the frequency of thrombocytopenia decreased
c) the scores on the Health Related Quality of Life scales improved and were related to reduction of aPL antibodies
d) in patients whose INRs had been going up and down with no real relationship to their anticoagulant dosing (a "sawtooth curve"), at approx. 3.2 months on HCQ this "bouncing around" smoothed out, consistent with aPLs going away.

These factors deserve more study.

**Why Haven't There Been (And Likely Won't Be) Large Prospective Randomized Controlled Trials of HCQ in APS?**

Because this drug has been available as a generic (a non-brand-specific name) for years, and has been used in lupus for years with FDA approval, there has not been the interest on the part of the several manufacturers worldwide to support a randomized controlled trial of HCQ to see if it prevents blood clots and lowers aPL antibodies.

**Other Literature That Supports HCQ Use.**

The Canadian HCQ Study Group showed years ago that when patients with SLE stopped their HCQ, they had flares of their disease. This began the caution to patients that continued use of HCQ was beneficial, and stopping HCQ could be harmful. Using a valuable patient sera and data bank from the military, Dr. McLain and her colleagues noted that when the blood of patients with SLE were examined for aPLs long before they had their diagnosis, and also before they had an aPL-related problem such as a thrombosis, the aPLs were present in their sera an average of 3-5 years before events. In Israel, Dr. Toubi showed that the addition of chloroquine to SLE patients' standard therapies was associated with a decrease in their aPL antibodies. Dr. Erkan and colleagues at Hospital for Special Surgery looked back at their patients and showed in a cross-sectional study that HCQ usage did appear to be protective against thromboses, as Dr. Petri's previously mentioned work had shown.

> **"Its low cost, low adverse event profile, and high efficacy make (HCQ) worth considering early in the course of APS with and without SLE."**

Dr. Costadoat-Chalumeau and her colleagues in Dr. Jean Charles Piette's group recently showed that when actual HCQ levels were measured in patients, low levels were associated with, and predictive of, lupus flares. They make the case for looking more carefully at actual levels and understanding what factors have to do with how different levels are achieved in different patients.

HCQ is a very safe medication, should be used with caution in patients with G6PD deficiency, requires no chronic or frequent monitoring blood work, but does require periodic ophthalmologic exams with color vision assessment. In the past, because of concerns with HCQ affecting the formation of the retina in babies, it was stopped for 3 months prior to a patient pursuing pregnancy, but data from many groups (reviewed in Wallace) now show that for SLE/APS patients, it is no longer necessary to stop HCQ for pregnancy or breastfeeding. Its low cost, low adverse event profile, and high efficacy make it worth considering early in the course of APS with and without SLE.

**Exciting Developments Using Patient Antibodies and Mouse Thrombosis Models.**

Dr. Pierangeli and colleagues are continuing to use their mouse models of APS to look at exactly how markers on endothelial cells (blood vessel lining cells) and platelets (the major blood-clotting cells in the body) change when human aPL antibodies introduced. These molecular markers and receptors on special cell surfaces are over-expressed from normal, a condition called "being up-regulated", which can promote clotting. Some of these newer biomarkers show changes when HCQ is present. . Her lab is developing new extensions of these mouse blood vessel injury models to understand just how both old (eg HCQ) and new (biologic response modifiers, anti-platelet agents, molecular inhibitors that interrupt signaling pathways in cells) therapies act to prevent or interrupt how aPL antibodies of different types cause blood clots in small and large vessels. These studies mean that new and exciting approaches to APS prevention or therapy is in progress. Stay tuned and informed!

**REFERENCES:**

1. Erkan D et al: A cross-sectional study of clinical thrombotic risk factors and preventative treatments in APS. Rheum 41: 924 '03

2. McCarty GA, Cason TE: HCQ Rx in APS: time course of clinical improvement and aPL antibody changes over 4 yrs. Arthritis Rheum 43: Suppl 9: S1061, '04

3. McCarty GA, Cason TE: Use of HCQ in APS at 3 academic rheum. Units over 2 yrs: improvement in aPL titer and symptom management. Proceedings, VIIth Int. Congress on SLE, M17A, '04

4. McCarty GA, Cason TE: aPL reduction in patients treated with LDA and HCQ: recursive partitioning analysis of a large APS cohort. Clin Exp Rheum 25: P70, 19, '07

5. McLain M et al: The prevalence, onset, and clinical significance of aPLs prior to the diagnosis of SLE. Arth Rheum 50: 1226 '04

6. Toubi E et al: Quinacrine added to ongoing therapy attenuates aCL production in SLE. Lupus 12: 297 '03

7. Costedoat-Chalumeau N et al: HCQ levels are predictive of flares in SLE. Arth Rheum 54:3284 '06

8. Carter AE, Eban R, Perrett RD: Prevention of post-operative deep vein thrombosis and pulmonary embolism. Br Med J 1: 312-14, '71.

9. Roubey, RAS: Treatment of the antiphospholipid syndrome. Curr Opinion Rheum 14::238-42 '02

10. Edwards MH et al: HCQ reverses thrombogenic properties of antiphospholipid antibodies in mice. Circulation. 96:4380-4, '97

11. Petri M. Thrombosis and systemic lupus erythematosus: the Hopkins Lupus Cohort perspective. Scand J Rheum 25:191-3, '96.

12. Wallace DJ: Antimalarial therapies. Ch 59 in Wallace DJ, Hahn BHH: Dubois' *Lupus Erythematosus.* 7th Ed, Lippincott Williams Wilkins, Phila. PA 1152-75 '06

13. Pierangeli SS, Vega-Ostertag M, Harris EN: Intracellular signaling triggered by antiphospholipid antibodies in platelets and endothelial cells: a pathway to targeted therapies. Thrombosis Research. 114:467-76, '04.

# Quick Tips—When Getting a Prescription

**Submitted by: Tina Pohlman**

Understanding the importance your medication plays in your treatment will help you get the most benefit from your prescription. It is important to take an active role in your health care by working with your doctor, nurse, and pharmacist to learn as much as possible about your prescription.

When you are prescribed a new medication, ask your doctor or pharmacist the following questions:

- What is the name of the medicine? What is it supposed to do?
- Is it okay to substitute a less-expensive generic medicine for the name brand? Will it achieve the same effect?
- What is the dose of the medicine? Are there food, drinks, other medicines, or activities I should avoid while taking this medicine?
- What are the possible side effects of the medicine? What should I do if they occur?
- How many refills of this prescription can I get?
- What should I do if I miss a dose?
- What should I do if I accidentally take more than the recommended dose?
- Is there any written information I can take home with me? (Most pharmacies have information sheets that you can use as an at-home reference.)

When you pick up your medicine at the pharmacy, check to be sure it is the medicine you were prescribed by your doctor.

When your doctor prescribes a medication for you for the first time, make sure to tell him or her the following:

- The names of all medicines you are currently taking, including both over-the-counter and prescription medication. It is important for your doctor to know this information in order to prescribe the medicine that will be the most helpful.
- Any concerns you have about using your medication.
- If you are allergic to any medication or have had troubling side effects from a medication that has been prescribed to you.

During your treatment, you should schedule a follow-up visit to your physician in order to monitor your progress. Make sure to tell him or her:

- About any problems you are having with your prescription.
- About any side effects or problems you have had since starting to take the prescription.
- About any new prescriptions that another doctor may have given you and any over-the-counter medicines that you started taking since your last doctor's visit.
- How you are feeling since starting the medication.

Remember, quality matters, especially when it comes to your health.

*Source: Quick Tips—When Getting a Prescription*. AHRQ Publication No. 01-0040c, May 2002. Agency for Healthcare Research and Quality, Rockville, MD. http://www.ahrq.gov/consumer/quicktips/tipprescrip.htm

# APS Related Book Review

**Reviewed by: Seren Estrada**

Holden, Trina. Positive Options for Antiphospholipid Syndrome. Alameda, CA: Hunter House Publishers, 2003. 128 pages

- Triona Holden is a former BBC news correspondent, medical lecturer and health journalist. She has Lupus and lives in London, England.
- With forewords by Graham Hughes, M.D., FRCP, and Robert Roubey, M.D., the book discusses the basics about APS and is organized into chapters addressing blood clots, stroke, miscarriage, headaches, misdiagnosis, Lupus, testing and treatments, and the affects on the heart and brain.

*Positive Options for Antiphospholipid Syndrome* explains in detail the 'ins and outs' of APS for an audience of newly diagnosed patients who want answers in layperson's terms. It includes several personal accounts from APS sufferers, with whom the like can sympathize. In this book, Triona Holden's objective is to "*plow through the medical jargon, sift out the facts and present them so that they can be easily understood.*" The book also has an extremely positive tone, as the title suggests.

If you suffer from APS, or have a loved one who does, this book will give you uncomplicated answers and stories with relatively happy endings. Although it is an easy and enjoyable read, I found it to be excessively optimistic. I felt at times like I was reading a tribute to Dr. Hughes, and that it was suggestive that Warfarin could take one's problems away altogether.

Overall, it was a good read---just don't let the text get your hopes up with its claims that Warfarin is a cure-all.

# From the APSFA FAQ Page

### Can I eat Vitamin K rich foods?

**Yes, but consistency is the key.** Some general nutrition dietary guidelines are:

1) Maintain the same diet, eat the same types of foods you ate regularly unless otherwise instructed.

2) Consult your doctor regarding any diet changes.

3) Avoid "binge" and crash diets.

4) Consult your doctor before taking any vitamins, mineral supplements or new medications.

5) An excess of foods high in vitamin K could have an affect on your anticoagulation: Limit to 1 serving per day (1 cup raw or ½ cup cooked): Spinach, Turnip greens, Cucumber peel, Broccoli, Brussels sprouts, Green scallion, Cabbage, Mustard greens. Avoid eating parsley, kale, seaweed, and green tea.

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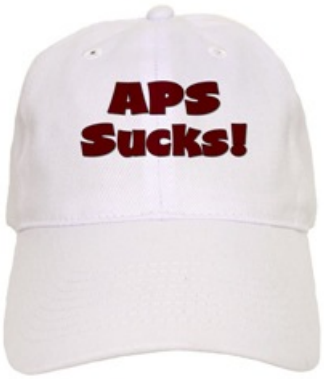
**APS Foundation of America, Inc.**

Our Mission Statement
Founded in June 2005, the APS Foundation of America, Inc. is dedicated to fostering and facilitating joint efforts in the areas of education, support, research, patient services and public awareness of Antiphospholipid Antibody Syndrome in an effective and ethical manner.

Sponsored by: Gundersen Lutheran · Marshfield Clinic — Where the future of medicine lives

## Have you seen our CafePress store lately?


We have hard at work creating some new, fresh designs for our CafePress store! We now have items available for the following syndromes or diseases which are related to APS: Vertigo, Sjögren's, Raynaud's, Stroke, TIA, Heart Attack, MS and Migraines. We have also added new designs to our Lupus, FVL and APS lines. Our CafePress items are high quality and the clothing comes in a variety of sizes from infant to many different adult sizes, including plus and maternity. Many items also come in a variety of colors. The APSFA gets to keep a small % of each sale from our store when you buy from it, so not only will you get a quality item, but you also make a donation to a worthy cause! Check out our store at the address below and be sure to check back often—we have more new designs in the works!





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