THE IMPORTANCE OF RESEARCH BLOOD
by Thomas A. Medsger, Jr. MD

Would you be willing to give two tubes of blood for research? We’re sure all of you have been asked this question when visiting our Scleroderma Clinic, probably most likely by the person pictured to the right and more than once!

What do we do with these blood samples? We are involved in a number of research projects using these specimens, as follows:

1. Antibody tests. As explained in several of our newsletters, 90% of systemic sclerosis (SSc) patients have 1 of 10 blood antibodies which are relatively specific to scleroderma (not found in other diseases). In 10% of SSc patients, none of these antibodies are found. Blood antibodies are useful because they are associated with features of disease such as the amount of skin thickening, muscle inflammation, lung and kidney disease. They are thus helpful in identifying patients at greater risk of developing these and other complications. Seven of the antibodies can be identified by commercial laboratories. The other 3 are detected in our Scleroderma Research Laboratory. We have encouraged one of the commercial labs to develop a “scleroderma panel” of all 10 antibodies which treating rheumatologists will be able to order in the future and which will be covered by medical insurance. Only 2 percent of SSc patients have more than one of these antibodies.

2. Antibody amounts. The amount of antibody in the blood is likely to be important. We have shown in the past that higher amounts of anti-Scl 70 antibody are associated with more active disease. One of our former research fellows, Dr. Masa Kuwana, and colleagues from Tokyo examined blood samples from SSc patients and found that higher amounts of this antibody were associated with more severe disease. They also noted that patients with higher antibody levels were more likely to have other complications such as lung disease.

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for anti-Scl 70 antibodies in samples from Japanese SSc patients at their first visit and 20 years later. Patients whose anti-Scl 70 antibody disappeared from the blood had less lung disease and improved survival after this 20-year period compared with those whose anti-Scl 70 antibody persisted in the blood.

We are currently collecting follow up blood samples in patients who initially had anti-RNA polymerase III antibody to determine what happens to the blood levels of this antibody over time and whether changes in antibody amount predict future events. Similarly, amounts of anticentromere and anti-Th/To antibody may warn us long in advance that a SSc patient may ultimately develop pulmonary hypertension, which occurs more frequently late in the course of disease when either of these two antibodies is present at the first visit.

3. Cytokines and chemokines. These are proteins which are produced by activated immune system cells in response to tissue injury and are important in the development of damage to blood vessels and tissue thickening (fibrosis) which are characteristic features found in tissues affected by scleroderma. When these proteins can be measured in the tissue or blood and can be shown to influence or predict disease complications or events, they are then referred to as “biomarkers”. In medicine today biomarkers are very important for clinical research, and are becoming increasingly useful in patient care. Dr. Robyn Domsic of our Center is interested in galectin-3 as a possible biomarker in scleroderma. She is looking to see if increased blood levels of the protein galectin-3 at baseline are associated with progression of skin thickening or lung fibrosis at subsequent visits.

4. T cells. Blood and affected tissues are sources of cells from the immune system, such as T cells and B cells. These cells can be separated out of blood, kept alive and studied. Dr. Fuschiotti of our Center has found that T cells from SSc patients with very active skin disease produce increased amounts of two cytokines, interleukin (IL) 13 and GATA-3. Treatment approaches which target these “overactive” T cells have the potential to slow down or halt the disease.

5. DNA. Heredity is an important predisposing factor in development of connective tissue diseases (CTDs), including SSc. Genetic factors appear to be more important in rheumatoid arthritis and lupus. We have reported that African-American SSc patients have a significantly different antibody profile compared with Caucasians. For example, anti-U3RNP antibody is common in African-American patients (35%) and uncommon in Caucasian SSc patients (5%). Anti-U3RNP antibody is associated with muscle involvement, heart muscle involvement and pulmonary hypertension. Genetic differences between African-American and Caucasian SSc patients undoubtedly play a role in these differences. Our Center is a contributor to a multicenter study collecting DNA samples and examining the genetic characteristics of African-American SSc patients.

6. Future projects. We frequently collect and store blood samples for later use even though we do not have specific studies in mind. As researchers identify new areas of interest, these samples from various stages of disease are very important to have available for examination. Our freezers now contain over 10,000 samples on over 3,000 SSc patients collected over the past 50 years.

In the future we also plan to collect blood samples from “normal” individuals, particularly those who do not have a CTD and who do not have a first degree relative (parent, sibling or child) with a CTD. For example, the spouse of a patient (not related genetically) is often an ideal “normal”. Studying the blood samples of normals gives us information on how SSc patients differ from normals and by what magnitude. Don’t be surprised if we ask one of the people accompanying you to the Scleroderma Clinic if he/she would be willing to “give us two tubes of blood”.

Although blood antibody testing is less useful in patients with localized forms of scleroderma (morphoea, linear scleroderma, fasciitis), all of the other information listed above applies to localized scleroderma as well. Dr. Kathryn Torok of our Center studies both childhood and adult onset localized scleroderma. She needs your blood also!

Our Scleroderma Center investigators greatly appreciate the willingness of our patients and family members to participate in these and other forms of research, including completing questionnaires pertinent to their disease. Without research, we will not be able to progress toward the goal that all of us have, identifying the cause/causes of these potentially devastating diseases and finding their cures.

Have A Big Heart...
Give Blood
Annually, the Scleroderma Foundation (SF) hosts a 3-day conference devoted to the education of patients, family members and health professionals who deal with scleroderma patients. Some of you have gone to this conference in the past. This year’s meeting was held in Anaheim, CA (near Disneyland) on July 25-27, 2014 and attracted over 500 attendees.

The University of Pittsburgh and UPMC scleroderma Canter was well-represented in the conference activities. The Grand Lecture, opening the formal portion of the program, was given by Dr. Robyn Domsic of our Center on pulmonary hypertension (PH), a topic of her clinical and research interest. In her presentation which was directed to patients, she reviewed the different types of PH, their symptoms, recommendations for screening of SSc patients for PH, the increasing number of treatment options now available for SSc-PH and the importance of multidisciplinary care for these patients. I wanted to approach the podium to congratulate Dr. Domsic on an outstanding lecture, but she was besieged by questions – the best sign of a successful presentation!

Dana Ivanco, our Scleroderma Research Coordinator, presented a well-attended session on “What You Can Do to Help Manage Your Disease”. She emphasized practical information that patients should know to maximize their knowledge of the disease, testing, medications and self-improvement strategies. I held a workshop on “Classification and Staging of Scleroderma Using Skin Thickness and Blood Antibodies”. Even after this slow-paced, interactive session, I got the impression that there is considerable confusion among patients and family members about disease subtype (diffuse vs. limited), disease stage (early vs. late), the risks of internal organ involvement and benefit of knowing which SSc-related antibody a patient has.

Several of our formal faculty members had prominent roles in the conference. Dr. Virginia Steen, who studied scleroderma at Pitt from 1980-1995 (now at Georgetown University in Washington, DC), received a Lifetime Achievement Award from the SF. This is the highest honor which can be given to a physician or basic scientist who has devoted his/her career to the study of scleroderma and who contributed significantly, both nationally and internationally, to patient care, teaching and research progress the understanding of the disease. Congratulations to Gini!

Janet Poole is a “regular” at the SF annual conference, where she talked about “Hand and Face Exercise and Management of Daily Skills” from her viewpoint as an expert in the occupational therapy approach to SSc.

For the first time, a Scientific Poster Session was held in which 4 x 6 foot posters were hung describing scleroderma research projects in lay terms. Thirty such posters were “presented” during a 2 hour session in which patients and health professionals had the opportunity to look at the poster panels and discuss the results with the authors. The Pitt contribution was to describe the ongoing multicenter trial of Rituxan (a B-cell blocking drug) for the treatment of SSc-PH (see photograph).

Before the formal conference, the SF hosted a one and one-half day session devoted to “new” or “young” investigators, most of who had received research grant funding from the foundation. At this New Investigator Conference, 12 young investigators had the opportunity to present their research findings and to receive...
feedback and suggestions from a panel of established researchers in both SSc and localized forms of scleroderma. Dr. Carol Feghali-Bostwick, who recently left Pitt last year to accept an endowed professorship at the Medical University of South Carolina in Charleston, was one of the organizers of this event. She serves as vice chair of the SF’s National Board of Directors and chairs its Research Committee. I “moderated” one of these sessions. I can say with confidence that they were highly informative for both established and junior level researchers and brought a sense of “community” to those who do, and those who aspire to do, high quality scleroderma research. Many of the young investigators were impressed by the genuine interest that established investigators showed in their projects and the highly useful feedback they received regarding suggestions for changes in research strategy, practical advice regarding applying for research grants and offers of research collaboration.

PEDiATRIC PATIENT ATTENDS SCLERODERMA FOUNDATION PATIENT EDUCATION CONFERENCE

Madison Gavin was 10 years old when her mom first noticed small patches of skin discoloration and thickening. After a dermatologist prescribed an ointment that did not help, a skin biopsy was performed and Madison was referred to the Children’s Hospital of Pittsburgh Scleroderma Clinic. There, they met Dr. Kathryn Torok, a pediatric rheumatologist, who thoroughly examined Madison and explained the diagnosis, prognosis and management to Madison and her family. Madison’s Mom, Angela, remarked, “Dr. Torok is a Godsend. She is truly a wonderful doctor who takes time with you. We consider her our very special friend.” Dr. Torok said, “Madison’s attitude is awesome and her smile lights up the room. Her family is very supportive and I am honored and privileged to be a part of her care.” When Dr. Torok suggested that Madison and her mother attend the SF patient education conference, they knew it would be a worthwhile event.

When asked how it felt to be at the conference with other kids with scleroderma, Madison said she didn’t think about the fact that they all had scleroderma. “I was just like every other kid there, so it felt normal.” She attended classes on yoga, making chocolate, art and music. She felt that the conference helped her realize that even though she might appear different than her classmates and peers, she is still “normal” and can do the same things that others can do. Knowing that there were others with the same problem, she didn’t feel different. Her mom noticed that Madison was at ease at the conference. Madison’s favorite part of the conference was meeting new friends. She hopes to attend next year to see everyone again in that educational and supportive environment.

“Stomping Out Scleroderma”

The 17th Annual Scleroderma Foundation National Patient Education Conference

July 17-19, 2015 Nashville, Tennessee

Registration opens late fall 2014 For more information and scholarship opportunities, visit: www.scleroderma.org/conference
We enjoyed a beautiful day at the fourth annual “Walk with Tori” scleroderma walk in Doubs Woods Park, Hagerstown, Maryland on September 14, 2014.

Attendees enjoyed the music of Take Two, May Novalis, and Brent Miller, who came from Nashville to support the cause.

All monies raised at the event are used for scleroderma research.

This year Tori and her team raised $33,000 making the total raised over the last 4 years over $140,000! We would like to thank all of the people who showed their support and joined us at the Walk!
The ABCs of CGAs

**Charitable Gift Annuities (CGAs)** are a great way to support the Scleroderma Center, while at the same time establishing a stream of income for you and/or a loved one. CGAs can be as simple as your ABCs. Here's a quick primer to help you understand the benefits.

**Always guaranteed income** – establish a simple agreement with the University of Pittsburgh and we provide you an income for life based on the size of your gift and your age.

**Balance goes to a program you care about** – the remainder of your annuity goes to help the work of the Scleroderma Center.

**Charitable deduction** – take an immediate tax deduction for a percentage of your gift and enjoy further tax benefits if you fund your gift through appreciated stocks.

Interested in learning more? Contact Gary Dubin at 412-647-9113 or dgary@pmhsf.org to get specifics on how a CGA might be the best fit for your charitable goals.

**CGA Examples**
The examples below are based on a gift of $10,000.

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