Being a physician has allowed me to meet many extraordinary people – my patients, their families, and their friends. This is a story of two of these extraordinary people and how friendship and love transcended the agony of illness. It is also a story of how the generosity of one person helped create the Johns Hopkins Vasculitis Center. I am glad to have the chance to tell you about both of these people, my patient, the late Mrs. Luvenia Jenkins, and her friend, Mrs. Esther Pearlstone.

I learned many important things about Mrs. Jenkins the day I first met her 12 years ago, when she was having a severe flare of rheumatoid arthritis. I learned that she was courageous and determined in the face of a crippling disease. I discovered her wonderful sense of humor, which was often punctuated by a devilishly joyful laugh. I also found out she could be stubborn: she refused to eliminate pickled pigs’ feet from what was supposed to be her low salt diet! And I learned that what made Mrs. Jenkins tick was being able to care for other people. She wanted nothing more out of her life than to care for others, especially her family and friends. Every time Mrs. Jenkins would come to the office she would look in my eyes and insist upon first asking how I was. When she left, she always said, “I am going to be fine. Don’t worry about me and get some rest.”

What I did not know in those early years was that Mrs. Jenkins had an extraordinarily devoted friend, Mrs. Esther Pearlstone. Mrs. Jenkins had worked in Mrs. Pearlstone’s home for many years and had helped take care of Mrs. Pearlstone’s two children. Over the years, they developed an abiding friendship that transcended an employer-employee relationship. When Mrs. Pearlstone saw that Mrs. Jenkins needed help, she did what she had done so many times before in her life – she devoted herself to making a difference at a personal and at a larger level.

I remember vividly the first time I received a telephone call from Mrs. Pearlstone. She introduced herself simply as a friend of Mrs. Jenkins. She expressed gratitude for the care Mrs. Jenkins was receiving and immediately wanted to know how (Continued on page 7)
A TEAM APPROACH TO TAKAYASU’S

The multi-organ system nature of vasculitis means that the best patient care usually requires teamwork by groups of experts. The following two stories of people with Takayasu's arteritis illustrate this point vividly:

Joie Hollis, a native of Bermuda, was 13 years old when her fevers and weight loss began. Little did she know that the cause of her symptoms, Takayasu’s, would remain undefined for a decade and a half. Over a period of several months, at a time of life when many young girls are going through growth spurts, Joie actually lost weight, going from 103 to 78 pounds. She also developed leg ulcers, and eventually required skin grafts. High doses of prednisone seemed to quiet most of her symptoms, but she remained without a diagnosis.

In the early 1990’s, Joie underwent an extensive evaluation in the United States. She was found to have mild narrowing of the artery supplying her right arm and slight enlargement of her ascending aorta — classic Takayasu’s findings. Still, no one linked Joie’s array of symptoms to that disease. In January 1998, Joie became progressively short of breath. It didn’t take long to figure out why. Her ascending aorta had become massively enlarged (see picture, lower left), leading to “wide-open” aortic valve regurgitation and massive backflow of blood into her lungs.

Joie was then taken to Baltimore for an urgent evaluation at Johns Hopkins, where a team of physicians set to work:

- Dr. Larry Griffith, the attending Cardiologist, suspected a rheumatologic problem and consulted the Vasculitis Center
- Dr. John Stone evaluated Joie and concluded that Takayasu’s arteritis had likely been the cause of her problems for 15 years
- A team of Interns, Residents, and Cardiology Fellows prepared Joie for surgery — now the only option for her badly damaged heart and aorta
- An echocardiographer, Dr. James Weiss, carefully assessed her cardiac function prior to surgery. Radiologist Dr. David Bluemke and angiographer, Dr. Aravind Arepally, performed imaging studies of her large arteries to help plan Joie’s operation
- In a heroic operation, cardiac surgeon Dr. Mark Redmond replaced Joie’s aortic valve and part of her ascending aorta with prosthetic materials. Simultaneously, he bypassed 2 coronary arteries that had been damaged by Takayasu’s.

Joie’s operation was a resounding success. To treat her Takayasu’s after Joie’s recovery from surgery, Dr. Stone placed her on methotrexate and tapering doses of prednisone. Several months after her operation, Joie Hollis became Joie Hollis Trott (see wedding photograph). Three years after her diagnosis and the start of her treatment by the team of Hopkins experts, her Takayasu’s remains in complete remission.

Normal aorta (on left) shown at angiography. At right, is Joie’s massively dilated aorta, before surgery.
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Mary Arendt was first evaluated by Dr. Michael Regan in January, 2000. Her symptoms had begun 2 years earlier, with profound fatigue. After several months, she had developed a constant pain in her chest - a dull ache behind her breastbone, accompanied by occasional sharp pains between her shoulder blades. Of all her symptoms, the most puzzling was her inability to blow dry her hair: holding her arms above her head quickly led to debilitating weakness.

When Dr. Regan first evaluated Mary, she had been taking 20 milligrams of prednisone a day for several months, with no clear diagnosis. When Dr. Regan examined the areas over large arteries in her arms, legs, and abdomen with his stethoscope, he detected bruits (“brew eez”) (whooshing sounds made by turbulent blood flow through narrowed blood vessels). The occurrence of these findings in such a young woman led Dr. Regan to suspect that Mary had Takayasu’s arteritis. This clinical suspicion was confirmed by a magnetic resonance angiogram (MR), performed by Dr. Bluemke. Convinced of her diagnosis and satisfied with her disease control, Dr. Regan began to taper her prednisone, adding mycophenolate mofetil (Cellcept®) to help decrease her prednisone requirement.

On subsequent MR studies, a problem appeared: the development of a lung nodule (see Figure). Lung nodules are distinctly unusual in Takayasu’s. Mary’s lung nodule grew larger and became “cavitated” (hollowed out). Dr. Regan consulted two colleagues about Mary’s problem: Dr. Rex Yung (a pulmonologist) and Dr. Malcolm Brock (a thoracic surgeon). Ultimately, an outpatient biopsy of the nodule determined that the cause of the lesion was an infection, Mycobacterium avium-intracellulare, a relative of the organism that causes tuberculosis. Fortunately, this common complication of immunosuppressive treatment responds to antibiotics, and is curable.

Mary now follows up regularly with Dr. Regan in the Vasculitis Center and Dr. Yung in the Pulmonary Clinic. Her lung infection has resolved nearly completely with combination antibiotic therapy. And with her Takayasu’s arteritis under excellent control, Mary is feeling her best in years.
Because I have vasculitis, is there any special diet I should be on?

We wish that controlling vasculitis were as easy as simple dietary manipulations (or even extreme ones!) Our patients would eat truckloads of carrots, radishes, macaroni & cheese, shoo-fly pie, and just about anything else if doing so would control their disease. Unfortunately, there is very little indication — and no solid evidence — that changes in diet affect inflammatory diseases such as vasculitis.

Our dietary advice to patients with vasculitis is practical, and designed to avoid compounding the side-effects of prednisone (See Clinic Corner, page 8). Many vasculitis patients take prednisone for prolonged periods of time, with side-effects that are well-known (weight gain, redistribution of body fat to undesirable places, “moon face”, high blood pressure, tendency toward diabetes, etc.) Consequently, we advise vasculitis patients to adhere to diets similar to those recommended for patients at risk for heart disease; specifically, balanced diets, low in fat and cholesterol, with adequate quantities of fruits and vegetables. By following these recommendations, people with vasculitis can go a long way toward insuring their own good health.

Will my vasculitis return?

After patients achieve remission from their vasculitis, it is logical for them to wonder if their disease will ever return. The answer, which is often difficult to give with certainty, depends in large part on the patient’s specific type of vasculitis. For example, some types of vasculitis, such as Henoch-Schönlein purpura (HSP) or vasculitis caused by a medication, tend to be self-limited and resolve on their own. Other forms of vasculitis (e.g., Buerger’s disease, a disease strongly associated with cigarette smoking) resolve with institution of the definitive treatment: smoking cessation. Still other forms behave less predictably, never coming back in some patients but demonstrating a tendency to recur eventually in up to half or more of all cases. Wegener’s granulomatosis, giant cell arteritis, Takayasu’s arteritis, microscopic polyangiitis, and other types of vasculitis fall into the category of diseases that often “flare” following the achievement of remission. Sometimes flares occur when patients go off of their treatments. Other times vasculitis flares when treatments are lowered in attempts to avoid side-effects.

At the present time, the ability of doctors to predict who will suffer disease flares and who will maintain in long-term remissions (or be cured) needs refinement. Progress in this area will come through research. Work in proteomics recently begun by the Vasculitis Center (see story on p. 6) may eventually contribute toward making prognostication in vasculitis more of a science than an art.

In guarding against the occurrence of a disease flare, what should patients watch for? We believe that several points are worth keeping in mind:

First, the symptoms of flares are usually very similar to the ones patients had when their diseases began. If headaches signaled the beginning of giant cell arteritis before, then the recurrence of headaches may indicate a disease flare. If leg ulcers began as painful red lumps on the leg the first time, then the return of painful red lumps may mean that vasculitis is back. Patients must become experts about their own manifestations of vasculitis so that they can recognize them immediately, consult their doctors, and begin appropriate treatment before serious damage occurs.

Second, patients must learn to know their own bodies, and report to their doctors any feelings or findings that are unusual. New symptoms may not only indicate a vasculitis flare, they may also herald complications of treatment such as infections.

Finally, because vasculitis treatments require careful monitoring by doctors, patients should discuss any changes in treatment with their physicians. Increasing or decreasing medications without consulting a physician may lead to trouble.
As providers of care for people with vasculitis, one of our greatest pleasures is seeing our patients busily engaged in the business of living, away from the hospital and engaging in activities they enjoy. Below are pictures of some of our patients doing just that:

**Diane Arke** and her husband, Edward, with their two children, Raymond and Catherine, at home in Pennsylvania.

**Paul Smith** with the pride and joy of his life, his 3 year old grandson, Eric.

**Lloyd Johnson** with his wife, Virginia, on a trip to Norway.

**Mrs. Stuart Graham** with her three granddaughters.

**Sheri Schwar** and her husband, Ron, on their wedding day, September 5, 1998.

**Aretha Mclain** with her son, Tony, and daughter, April, at a spring wedding.

**Stacey Labahn** at the wedding of a friend, Jiwon Kim, in the fall of 2002.

**Melvin Tobery** spending quality time with his two great-grandchildren, Jake and Cheyenne, in Frederick, Maryland.

**Peter Benac** with his cherished family: Heather, Sheila, and Todd.

**Glenda Cole** (left) at the 30th birthday of her daughter, Washonda.

**Mary Glyde Seivard** with her husband Louis at her 60th high school reunion.
Proteomics: The Clinician’s Tea Leaves?

The ways that many vasculitis treatments work remain poorly understood. New research at the Vasculitis Center may yield insights into the mechanisms of the drugs used to treat vasculitis. This in turn may lead to safer and more effective therapies for patients with inflammatory vascular disease. The following story illustrates how a novel research technique may one day impact patient care in important ways.

A.N. first developed fevers in 1987, when he was a senior in high school. After a year during which the fevers came almost every day, the fevers resolved mysteriously on their own. But the disease returned with a vengeance during A.N.’s senior year at Georgetown University, sometimes so severely that he required hospitalization. The fevers, as high as 104°F, responded only to treatment with steroids (prednisone). A.N. also developed skin ulcers (see picture), purple toes, and muscle weakness. He lost parts of several toes on the left foot because of severely inflamed blood vessels. Eventually, skin and nerve biopsies led to the diagnosis of a specific form of vasculitis, polyarteritis nodosa (PAN).

Although high doses of prednisone helped keep A.N.’s PAN under partial control, side-effects of the prednisone mounted. A.N. gained weight and developed fragile skin from his prednisone. Cataracts grew in his eyes and he showed signs of early diabetes. His bones became thin (at the age of 30, A.N. was diagnosed with osteoporosis), and his muscles weak. And unfortunately, despite all the prednisone, his PAN remained active. Fevers continued to occur intermittently, new skin ulcers developed, and his nerve symptoms progressed, leading to difficulty with walking.

Finally, in 1999, A.N. was put on cyclophosphamide (Cytoxan®) by physicians at the Vasculitis Center. Remarkably, his fevers vanished. Within six months, his skin ulcers had healed and he was able to discontinue his pain medication completely. For the first time in nearly 10 years, he no longer required prednisone. The weakness in his feet improved dramatically. He was able to jog again, and even to play basketball. In short, cyclophosphamide had saved him from the disease which, along with its toxic treatment, had slowly been killing him.

How did the cyclophosphamide work? What “evil humors” within A.N.’s immune system did it suppress? And — most important to A.N. — will his PAN return now that he is off the medication? Despite the fact that cyclophosphamide was first used to treat vasculitis half a century ago, the answers to these questions remain unknown. Cyclophosphamide, a drug initially designed as a chemotherapy for cancer, is perhaps the strongest medication used to treat inflammatory disorders of the immune system. The drug affects hundreds (if not thousands) of molecular targets within the body indiscriminately, suppressing many “good” and “bad” elements alike. Though frequently effective, suppression of the “good” elements may cause major side-effects. For example, 42% of patients who take cyclophosphamide for prolonged periods suffer permanent damage related to this treatment. Precise understanding of the good and bad effects of cyclophosphamide would be an enormous step forward, allowing the design of more rational and safer treatments.

New research at the Vasculitis Center may help provide answers. In collaboration with colleagues at the National Cancer Institute and the Food and Drug Administration, Vasculitis Center investigators are exploring the cutting-edge technology of proteomics, the study of blood proteins. Early studies in proteomics have been conducted in cancer. This initial work indicates that one day — a day very soon — simple blood tests may permit doctors to distinguish accurately

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between ovarian cancer and benign ovarian cysts. Preliminary applications of this technique to vasculitis are shown in the figure below:

The top panel shows a protein profile from the blood of a patient with active Wegener’s granulomatosis. Notice the two middle peaks in this panel (arrows). In the lower panel, a protein profile from the same patient 6 months later during a period of remission, these two peaks — each representing a specific protein — are entirely gone. Using the most recent research techniques, the identities of these specific proteins can now be discovered. Further application of proteomic techniques to blood samples from patients with vasculitis may yield insights into the precise types of molecules that contribute to vascular inflammation. We will report on this work in upcoming issues of the newsletter. Proteomics studies at the Vasculitis Center are funded in part by a grant from the Maryland Arthritis Research Consortium (MARRC).

Epilogue: A.N. has now been off of cyclophosphamide for one year. His vasculitis remains in remission.

The Eternal Gift: Continued

Pearlstone had moved to Colorado, she flew back frequently just to spend time with Mrs. Jenkins. She would sit with Mrs. Jenkins, talk with her, listen to her, and hold her. Whenever Mrs. Jenkins had to be admitted to the hospital, Mrs. Pearlstone would send beautiful flowers and plants to brighten her room. As Mrs. Jenkins became increasingly disabled (the treatments were not as good then as they are now), she was most frustrated by not being able to do what she most enjoyed – helping and serving others. Gradually, she came to realize that through her friendship with Mrs. Pearlstone, they had formed a partnership that was very much helping many people by advancing research. So, in a very real sense, Mrs. Pearlstone’s gifts not only helped us advance research, they also helped Mrs. Jenkins feel that she was valuable and contributing to society. I have no doubt that their “partnership” in helping people allowed Mrs. Jenkins to deal bravely with the progression of her disease.

When Mrs. Jenkins died several years ago, Mrs. Pearlstone was at her side. Today, Drs. Antony Rosen, Dr. John Stone, and the entire staff of the Vasculitis Center continue to try to turn the spirit of the friendship between Mrs. Jenkins and Mrs. Pearlstone into an enduring legacy to benefit all people.
Clinic Corner: Minimizing Prednisone Side-Effects

Prednisone is the swiftest-acting and one of the most powerful medications that we have to treat vasculitis. The higher the dose, the greater the effectiveness of prednisone – and the higher its likelihood of side-effects. The following tips can help minimize some of prednisone’s most common side-effects:

1. Take prednisone in the morning and with food. Morning administration mimics the body’s own natural production of steroid hormones, and will make it easier to stop prednisone eventually.
2. Don’t be alarmed by thrush. This minor yeast infection in the mouth can usually be treated easily by over-the-counter or prescription anti-fungal medicines.
3. Guard against other types of infection. Patients on high doses of prednisone for prolonged periods of time may need to take medicine to prevent a type of pneumonia that may complicate treatment.
4. Protect your bones. Daily calcium, vitamin D, a bisphosphonate (etidronate, pamidronate, risedronate, or alendronate), and/or calcitonin may all be appropriate to protect against bone-thinning (osteoporosis).
5. Do your best to push away from the table. Pushing away is not easy, because prednisone often causes a substantially increased appetite. Therefore, most patients gain weight with prednisone. But remember: these effects are reversible, and will go away as the prednisone dose is lowered.
6. Monitor your blood sugar and blood pressure carefully. Prednisone can raise both. Blood sugar levels and blood pressure should therefore be measured regularly, particularly if these have been problems in the past.
7. Remission is the sweetest revenge. The surest way to minimize the side-effects of prednisone is to put the disease into remission and get to a lower dose. Most patients with vasculitis are eventually able to decrease their prednisone doses to tolerable levels. In time, many even stop prednisone completely. The day prednisone is stopped is a day to celebrate, for patient and physician alike!