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Of Ears and E-mails

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The news came via e-mail. *"Well, the day has come. Last week, while visiting my friend Andie in Cincinnati, my right ear started to change and slowly my hearing aid has become useless. I am now profoundly deaf... I'm O.K. with that — as much as one can be; I've had 4 years to prepare."* With that Internet message to me and my colleague, Howard Francis, an ENT (Ear/Nose/Throat) doctor, Stacey informed us that our efforts to preserve her hearing had failed. During the time I had been her doctor, I had admired much in

Stacey. Feeling utterly powerless in the wake of her e-mail, I realized then that my admiration for her had only begun. Once again, a patient was teaching me a lesson in strength.

When I met **Stacey Labahn** — now some 67 doctors' visits ago — she had suffered from a puzzling ailment for several months. In 1998, she had suffered frightening paroxysms of vertigo and hearing loss, followed by redness and swelling of her right eye. The rapid and severe onset of her symptoms forced her

to take a temporary leave of absence from her job as a software marketing executive. This constellation of symptoms had led to the tentative (and incorrect) diagnosis of Wegener's granulomatosis. Despite the difficulty of pinning a definitive name on her problem, Stacey had been improving on treatment. We labored together



Pauline Marler Stone (seated), teaching deaf children, circa 1928

Of Ears and E-mails: Continued

(Continued from page 1)

without a clear diagnosis for months, but in time were able to taper off her potentially dangerous therapy. The medications helped return her hearing nearly to its pre-illness level and, to my relief, caused this bright, energetic woman no harm.

I quickly developed an attachment to Stacey. Her take-charge, “just-the-facts” approach to dealing with her strange, sudden illness caught my attention for its lack of self-pity. Stacey was used to making things happen in her life; in her work, she analyzed clients’ business problems and found solutions. Applying the same troubleshooting concepts to her illness that she had used in business, she was going to figure this out, put it behind her, and move on.

We connected on several levels. First: there was the computer. The Vasculitis Center website had just been launched. Stacey gave me advice about our webpage and created her own: the Vasculitis Education Center (<http://groups.yahoo.com/group/vasculitis-ed-center>), an accumulation of articles and websites related to vasculitis that she had found helpful in coming to grips with her problem. Though she could still hear then, she was the first of my patients to teach me the efficiency of communicating via e-mail.

Second: there was food. When traveling, I discovered there was no better way to find a good restaurant than to ask Stacey. Working in the software industry had taken her all over the country and given her many chances to try local foods. Checking my e-mail from San Francisco, New Orleans, or elsewhere, it was not unusual to find in my inbox a file containing the latest on the best places to eat, complete with reviews. I was impressed, amused — and touched.

Third: there was our ages. I was 35 when I became



From left to right: Dr. John Stone, Stacey Labahn, Dr. Howard Francis

Stacey’s doctor, and she 33. For any physician, it is a revealing experience to encounter a patient one’s own age. This is particularly true for a young doctor. For years in their early training, doctors spend most of their time caring for patients older than they are — often much older. Until they learn better, young doctors sometimes view patients’ illnesses abstractly: sickness is something that happens to people later in life — years later. Stacey and I had watched the same TV shows as kids, gone to similar public schools, and though living in different parts of the country, experienced the world through the eyes — and ears — of the same generation. Now, my profession and her unexpected illness had caused our parallel tracks to merge. Such experiences not only affect patients’ lives profoundly, they are sobering and formative for physicians, as well.

After months of remission, her dizziness and hearing problems returned. This time, the symptoms were accompanied by an eye problem that revealed the correct diagnosis. Over the telephone — still hearing, now with the help of hearing aids — Stacey said that her eyes had become red and sensitive to light. She suspected allergies. I had her evaluated immediately by colleagues in Hopkins’ Wilmer Eye Institute, where “interstitial keratitis” — inflammation within the lens of the eye — was diagnosed. Instantly, the pieces of the puzzle fell together in a way that finally made sense: Stacey had **Cogan’s Syndrome** [See Box, page 3-4].



Stacey’s Eye: Clouding over the top part of the “iris”, indicative of keratitis.

Her case developed a familiar pattern: vertigo and hearing loss — treatment — improvement — remission — residual hearing deficit — repeat. Dr. Francis and I observed that each post-treatment audiogram revealed that her hearing thresholds had declined another 10 or 20 decibels. We attempted just about everything to save Stacey’s hearing: steroids (again), cyclophosphamide (again), mycophenolate mofetil, etanercept, infliximab —

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even injections of steroids behind her eardrum. We agonized over each treatment decision, worrying all along that in our attempts to help, we might do more harm than good. With each flare of her disease, more and more of Stacey's hearing was lost.

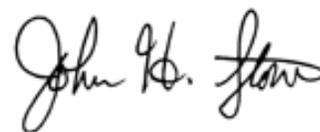
As Stacey's hearing declined, I recognized another connection between us. My great Aunt Margie, now gone, had lost her hearing at the age of 2. Family lore has always held that her deafness resulted from the flu epidemic of 1918. Afflicted as a toddler, Margie lived for more than 70 years in a world of silence. Inspired by Margie's challenges, her 18 year old sister — my grandmother — traveled from a small town called Prosper, Texas to a big city: St. Louis. There, at the Central Institute for the Deaf, "Mums" learned her life's vocation: teaching deaf children. A treasured family picture (see page 1) shows Mums as an apprentice teacher, playing the piano for a class of deaf children at the Central Institute. The students' hands rest on the wooden piano surface so as to feel vibrations from the chords they could not hear. I showed Stacey the picture and communicated its tale by writing the story of Margie and Mums on a legal pad.

Stacey accepted the possibility of deafness long before her doctors did. Even while trying to prevent what became inevitable, she prepared. I marveled at her lack of self-pity, a reflection of her remarkable strength. At each appointment, she informed me of her growing network of hard-of-hearing and deaf friends, her progress with the daunting new skills of lip-reading and sign language, her deliberations about cochlear implants [see pages 8-9]; in short, about her growing immersion in the proud world of the Deaf. Once, she brought to clinic a bag of homemade cookies for me. Within the bag was a simple picture of a man signing "Thank you".

Losing her hearing has altered Stacey's life in ways that I could not foresee 5 years ago. She lost one high-powered job and then another, and is now on temporary disability. She has changed cities. Music is but a memory. She can no longer use her cell phone or a pay phone, but communicates continuously via e-mail. E-mail, she observes, is a

blessing, yet it lacks the immediacy of picking up the phone and speaking to a friend. She is becoming familiar with Voice Carry Over and TTY (Teletypewriter) technology, breakthroughs that now increasingly permit deaf and hard-of-hearing people to use telephones.

One contrast between our once parallel tracks is striking. On many days, I arrive at my office and sigh at the number of e-mail messages already awaiting replies. For Stacey, those are the beginnings of a full day of conversation, heard with her eyes and told with her hands.



From Stacey: "Over the last five years, I've worked with many departments and many physicians at Johns Hopkins. In my illness, I have been very lucky to have The Vasculitis Center as a resource. My treatment is both astounding and reassuring to me. Even though we have lost the battle with my hearing, the care, patience, and understanding I have received from Dr. Stone and Dr. Francis have enriched my life. Their work and willingness to apply new protocols and medications to my case made the difference between immediate deafness and the period of adjustment I was permitted for four years. I am extremely proud of my physicians and want to take this opportunity to thank them for all they have done and continue to do for me as a patient and person."

Cogan's Syndrome

Cogan's Syndrome was described first in 1945 by Dr. Daniel Cogan of the Massachusetts Eye and Ear Infirmary in Boston. Cogan reported four patients between the ages of 20 and 35 who presented with either eye problems, ear dysfunction, or both. The eye problems consisted of pain, redness, and sensitivity to

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light, resulting from interstitial keratitis. The ear dysfunction was characterized by disabling vertigo (caused by an inner ear malady) and progressive bilateral deafness. In Cogan's Syndrome, the eye and ear involvement can occur either simultaneously or be separated in onset by a number of months.

Compared to the ear disease, the eye inflammation in Cogan's Syndrome is usually easy to control with steroid eye drops. The hearing dysfunction, however, may require treatment with intensive immunosuppression. A substantial portion of patients lose their hearing, and some become completely deaf following repeated disease flares. In 10-15% of cases, a large-vessel vasculitis involving the aorta and its branches develops.

Cogan's Syndrome rivals all other forms of vasculitis for the mystery that surrounds it. The reasons that the eyes and ears are targeted so specifically in this disorder are not



Stacey Labahn & Dr. Francis

known. The nature of the ear problem is poorly understood because of the lack of accessibility to the inner ear. Located deep within the temporal bone of the skull, to open the inner ear to perform a biopsy is to destroy its function. Thus, doctors are essentially never able to observe what early, untreated disease looks like under the microscope, and therapies remain empirical.

One key to minimizing disability in Cogan's Syndrome is prompt recognition. The fact that the eye and ear symptoms frequently present at different times makes early diagnosis a challenge. The disorder is often misdiagnosed as something more benign, such as otitis media or benign positional vertigo. For patients with severely damaged hearing from Cogan's, however, help is on the way [see **Re-establishing Contact**].

May Flowers: New Faces in the Vasculitis Center



From left to right: D. Buxbaum, D. Pearson, D. Paul, L. Pinachos

We are pleased to announce that the arrival of Spring witnesses several new faces in the Vasculitis Center. New to the Vasculitis Center (or in new positions within the Center) are:

Lourdes Pinachos, RN

Lourdes is known to many patients and friends of the Vasculitis Center already: she has served as the trial coordinator for the Wegener's Granulomatosis Etanercept Trial (WGET) for the past year. In March, Lourdes became the Center's new Senior Research Coordinator. Lourdes, whom we featured in the Clinic Corner of the Fall, 2002 issue of the Newsletter, is a Registered Nurse who graduated from Catholic University in Washington, D.C. Before joining the Vasculitis Center, she worked at the General Clinical Research Center, an NIH-funded research core at Johns Hopkins Bayview. She brings to the Center great enthusiasm, a thorough organizational sense, important experience in human resource issues and, most importantly, a love of nursing.



In assuming the role of Senior Research Coordinator at the Center, Lourdes replaces Misty Uhlfelder, who has served in that role for 5 years and moves on now to a position in the Welch Center for Prevention, Epidemiology, and Clinical Research.

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Delphine Paul

Back in the Autumn of 2002, the Vasculitis Center scored an enormous coup by recruiting Delphine Paul from the downtown campus, where she had worked as a lead lab technician for 7 years. She has been a Hopkins employee for a total of 15 years. As the principal phlebotomist in the Center, Delphine organizes a group of phlebotomists and technicians who not only draw blood for clinical purposes, but also process research specimens for the Center’s ongoing protocols. Perhaps because of her self-confidence (born of drawing blood from thousands of people over the last decade and a half), Delphine has a calming influence on patients, putting them at ease for phlebotomy procedures – which are understandably stressful for many. We now say without reservation that we have under our roof the best phlebotomist in the world!



In the Vasculitis Center’s new space at Bayview, Delphine and her phlebotomy team replace “Express Testing” from the first floor of the Outpatient Center downtown. Delphine’s location, just around the corner from any examining room, is another advantage of the Center’s new space.

Danielle Pearson

With the possible exceptions of serving as a Marine in Iraq or as an intern in one of the Johns Hopkins hospitals, there is probably no tougher job anywhere than being a Patient Service Coordinator at the Vasculitis Center. Serving our patients with the alacrity, skill, and professional attitude they deserve (and have come to expect from Judy



Harrison and Chasity Wiener) is a job of which only a proud few are capable. Danielle Pearson is one of those. Along with Delphine, Danielle is another patient service superstar raided from the Johns Hopkins Outpatient Center. In a few short weeks, under the careful tutelage of Judy, Danielle has learned the ins and outs of patient scheduling, test ordering, phone call fielding, hospital admission organizing, prescription filling, and everything else accomplished by a Vasculitis Center Patient Service Coordinator in the course of a routine day.

Danielle assumes the job previously occupied by Chasity Wiener, recently promoted to another administrative role within the Rheumatology Division.

Denise Buxbaum

And speaking of Marines, we now have a bona fide, dyed-in-the-wool former “Lady Leatherneck” in the newly-created role of Research Data Assistant/Secretary. Denise Buxbaum, a Hopkins employee for five years, joins us from the Johns Hopkins Behavioral Pharmacology Research Unit. In her previous Hopkins roles, she has performed a variety of tasks that include grant submissions, database management, newsletter creation, physician scheduling, manuscript preparation, and others, all of which will serve her well in her new capacity as our Research Data Assistant Secretary. These include the preparation of this Newsletter, maintenance of the Vasculitis Center database, administration of the Center’s development program, the organization of Center meetings, and much, much more. Her cheerful, “can-do” attitude is a welcome addition to the Center.



Denise assumes many of the functions performed previously by Amanda Masterson, who recently returned to Colorado with her husband and new baby to raise her family closer to home.

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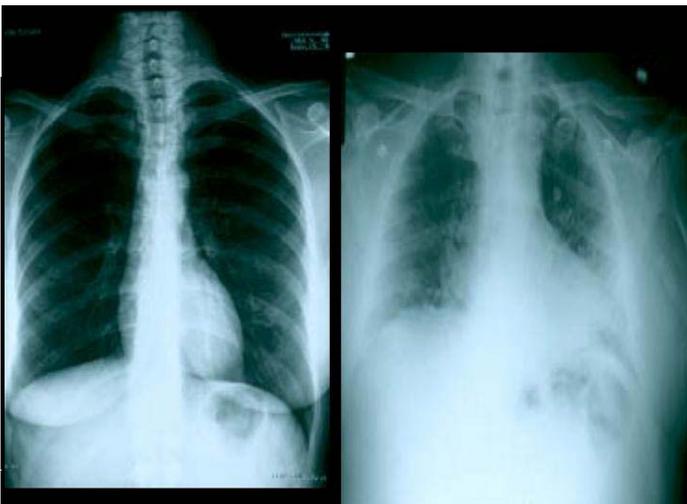
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And there are more new faces to come in the next few weeks. Over the summer, we anticipate hiring:

- A new Patient Service Coordinator to help with the growing number of patients who wish to attend the Center for evaluation.
- Another nurse to serve as a Research Coordinator for new clinical trials slated to begin in the autumn.

Frequently Asked Questions: "Methotrexate (MTX)"

Dr. Bruno Daminelli, a neurosurgeon from West Virginia, had enough of cyclophosphamide (CYC) the first time around. When diagnosed with Wegener's granulomatosis in 2000, he was treated with the combination of cyclophosphamide and



Normal chest X-ray (left). Dr. Daminelli's chest X-ray during the time he had pneumonia (right).

prednisone. Two months into treatment, he began feeling worse following a period of initial improvement. His doctors thought that his vasculitis had become refractory to therapy, and increased the doses of his medications. He was hospitalized for worsening pulmonary infiltrates [see above]. Just before his transfer to Hopkins, bronchoscopy revealed the true cause of his increasing breathlessness – an infection: *Pneumocystis carinii* pneumonia. Before the infection was controlled during a stormy two-

week course in the Hopkins ICU, it nearly claimed Dr. Daminelli's life.

When his vasculitis returned in 2001, Dr. Daminelli was understandably reluctant to resume treatment, even though as a physician himself he knew it was essential. He and his wife were both relieved when physicians at the Vasculitis Center recommended the use of MTX rather than CYC to induce disease remission this time. The combination of MTX and prednisone put Dr. Daminelli's Wegener's back in remission. He has now been off of prednisone for 18 months and his disease remains under control on MTX. In this series of FAQ, we review the role of MTX in treating some cases of vasculitis, and discuss ways to use this medication safely.

How is MTX taken?

Patients take MTX only once a week. Most of the time, MTX is administered by mouth. If oral administration is associated with nausea, subcutaneous or intramuscular injections can also be given.

Which types of patients are candidates for MTX?

MTX is reserved for "limited" (relatively mild) cases of vasculitis that do not pose immediate threats to either patients' lives or their vital organs. MTX is sometimes used as the primary remission induction drug (along with prednisone), but it is also used commonly after the discontinuation of CYC because of its superior side-effect profile. One common strategy is to use CYC for 3 to 6 months in individuals with severe forms of vasculitis, and then to switch over to MTX once the disease has been controlled.

Are there some people who cannot take MTX?

Yes. People with poor kidney function are not candidates for MTX. The drug is metabolized partly by the kidneys, and excessive risks of toxicity occur in patients with serum creatinine levels > 2.0 mg/dL. Patients with histories of some types of liver disease should also not take MTX. Because of its risk of causing teratogenicity (i.e., to induce birth defects or to cause abortion), MTX is also not used in pregnant women.

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What are the side-effects of MTX?

If appropriate precautions in prescribing the medicine are used, MTX is generally well-tolerated. Some patients experience mild nausea or queasiness for a day or so after taking the medication. Bone marrow suppression (low blood counts) can occur in some patients, particularly those treated before MTX with CYC. Inflammation in the liver may also occur.

Because of the bone marrow and liver problems that may develop in patients on MTX, regular monitoring of bloodwork is required; these complications are reversible if detected early. Another potential concern with MTX is “pneumonitis”, a type of inflammation that may occur in the lungs as a response to MTX. This side-effect, too, is reversible, as long as it is detected early. Finally, it is possible that some forms of cancer, particularly lymphomas, are more common in people who take MTX. The risk of cancer is far lower with MTX, however, than with CYC.

Do I need to take other medications with MTX?

Yes. Two types of medication are prescribed along with MTX. First, an antibiotic is given to prevent opportunistic infections that may occur with MTX (e.g., the *P. carinii* pneumonia that occurred in Dr. Daminelli’s case in association with CYC). The antibiotics we use are: 1) single-strength Bactrim daily; or 2) dapsone 100 mg/day.

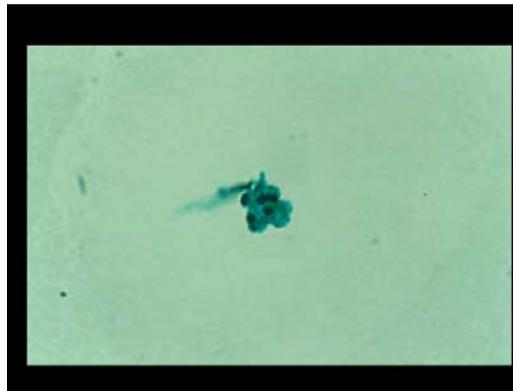
The second type of “medication” that patients on MTX should take is a vitamin – folic acid (1 mg/day). This vitamin helps prevent mouth sores that occur in some patients on MTX.

What other precautions do I need to take while on MTX?

Regular bloodwork – not less often than once a month – should include a complete blood count (white blood cell count, hemoglobin/hematocrit, and platelets), liver function tests (albumin, AST/ALT), and a test of kidney function (creatinine).

Can I drink alcohol while I am on MTX?

Some physicians say that patients on MTX can have one drink – at their daughter’s wedding! In general, patients on MTX must be extremely careful about their alcohol intake. More than one drink/week is probably excessive for most patients taking this medication. Up to one drink/week is permissible in most cases, provided that there is no change in patients’ liver function tests.



Pneumocystis carinii, the organism that caused Dr. Daminelli’s pneumonia

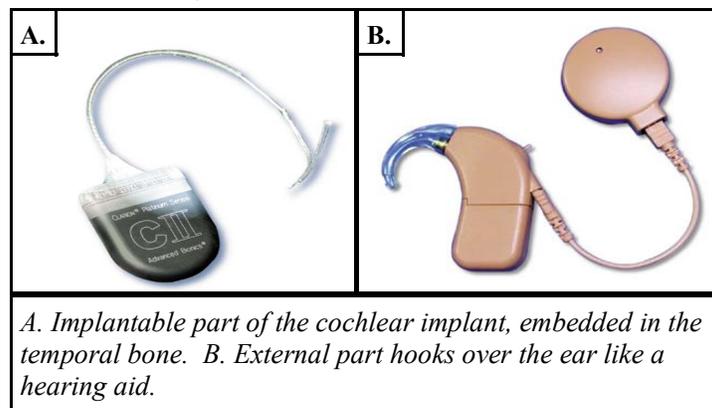
Using Methotrexate (MTX) Safely

FIVE THINGS TO REMEMBER WHEN TAKING MTX:

- Blood tests every month – and more commonly if your counts have been low
- Single-strength Bactrim or Dapsone 100 mg/day: keeps *Pneumocystis carinii* away!
(Only single-strength Bactrim should be used with MTX)
- Folic acid: 1 mg/day. Simple, over-the-counter vitamin may prevent mouth ulcers
 - Alcohol only in extreme moderation: ≤ 1 drink/week
- Alert your physician immediately if you feel sick. Cough and shortness of breath are major concerns for patients on MTX

Re-establishing Contact: Cochlear implants

Dr. Howard Francis, a medical school classmate of Dr. Stone's, is an Associate Professor in the Department of Otolaryngology at Hopkins. (Otolaryngologists are most often referred to as Ear, Nose, & Throat physicians). Dr. Francis evaluates patients with hearing problems, which frequently complicate Cogan's syndrome, Wegener's granulomatosis, giant cell arteritis, and other forms of vasculitis. In some cases of severe hearing impairment, Dr. Francis is able to restore functional hearing by performing a cochlear implant. This surgical procedure re-establishes contact between the auditory nerve – still viable in most cases of deafness – and sensory input from the hearing world. Dr. Francis answered some questions about this procedure below.



A. Implantable part of the cochlear implant, embedded in the temporal bone. B. External part hooks over the ear like a hearing aid.

What is a cochlear implant?

In deafness, some components of the ear's hearing apparatus are damaged beyond our current abilities in restoration. Cochlear implants, however, allow us to bypass the damaged parts of the ear and route auditory input to the place it needs to go: to the nerve that carries auditory data from the cochlea (the inner ear) to the brain.

In most cases of deafness, the auditory nerve that connects the ear to the brain still works perfectly well. But it is bereft of sound input from the outside world. The cochlear implant, a prosthetic device, is manufactured using state-of-the-art "microchip technology" [see two-paneled Figure, A and B]. The body of the device (A) is implanted within the temporal bone, just behind the ear. An external device that includes a microphone (B) gathers and delivers sound information to the hearing nerve of a deaf ear in the form of coded electrical signals. The implant transmits this information via a thin array of electrode wires placed inside the cochlea. Implantation

of this device requires less than three hours in the operating room, and is an outpatient procedure.

The clarity of hearing with cochlear implants is influenced by several factors, including the selected programming features of the speech processor (which may be adjusted), the duration of the patient's deafness, and the severity of hearing loss. Other unknown variables also appear to influence the effectiveness of cochlear implants.

Which patients are candidates for cochlear implants?

Cochlear implants are indicated for individuals who, even with hearing aids, are unable to understand most spoken conversation without visual assistance through lip reading, sign language,

or the written word. Most individuals in this situation have severe to profound hearing loss in both ears and score 40% or worse on standardized speech discrimination tests. Deafness in just one ear is not an indication for a cochlear implant (other interventions, such as hearing aids, are more appropriate in that scenario).

How much do cochlear implants improve hearing?

Cochlear implants produce significant increases in the awareness of sound in all patients, converting severe or profound hearing loss to mild hearing loss. The clarity of the resultant hearing and the ease with which speech is understood, however, vary among patients. Cochlear implants enhance verbal communication in the vast majority of patients who are selected appropriately for the procedure. The benefits include improved lip reading and, in about 60% of patients, a diminished need for visual cues in the understanding of speech. This allows many to use the telephone. As shown by a recent study from the

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Department of Otolaryngology at Hopkins, this increased social interaction is associated with a marked improvement in quality of life.

What's on the horizon for individuals with hearing impairment?

Hearings aids are getting better all the time. Both hardware and software developments promise to create more effective instruments for the amplification of sound. First, although still in their infancy, implantable hearing aids promise to provide better fidelity and power by transmitting amplified sound-induced forces directly to the middle ear bones. Second, a new type of hearing device that combines the acoustic stimulation of a hearing aid and electrical stimulation of a cochlear implant is now being tested. This device electrically stimulates the parts of the cochlea that are most profoundly deaf, but uses residual function in other parts of the same cochlea by presenting sound through an integrated hearing aid.

Finally, research is slowly revealing the mechanisms behind hearing impairment. More complete understanding of these mechanisms will lead to the availability of medications to combat deafness. My colleagues and I are developing tools with which current and future therapies can be delivered directly to the inner ear. One day, the combination of robotic technology, gene therapy, stem cell therapy, and good old-fashioned drug development will render deafness a curable condition.

Johns Hopkins University was created through the vision and philanthropy of one man, Johns Hopkins (1795 - 1873), a Baltimore shipping and railroad magnate.

If you are interested in knowing more about how you can support the mission of The Johns Hopkins Vasculitis Center in discovery, teaching, and patient care, please contact:

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Barcelona to Baltimore

We are also delighted to welcome Dr. Alicia Rodriguez-Pla to the Vasculitis Center from Spain. Dr. Rodriguez-Pla, a fully-trained Rheumatologist who recently completed her Ph.D. work in Barcelona, has come to Hopkins to perform a two-year post-doctoral fellowship in Hopkins' Stanley Neurovirology Laboratory. She was attracted initially to Johns Hopkins after reading of previous work done by Vasculitis Center investigators in the area of potential infectious causes of these diseases.



Mr. Joseph Gostin of Flushing, NY and Dr. Alicia Rodriguez-Pla

(Previous work, for example, has debunked the putative association between a bacterial infection – *Chlamydia pneumoniae* – and giant cell arteritis). Giant cell arteritis, a form of vasculitis that afflicts more than 160,000 persons over the age of 50 in the United States, holds a special fascination for Dr. Rodriguez-Pla.

Dr. Rodriguez-Pla will study the role of viruses as contributors to the development of giant cell arteritis. In the Stanley Neurovirology Laboratory, she will apply to her investigations a number of new techniques that provide unprecedented sensitivity for microbes. She will collect temporal artery biopsy specimens from the Wilmer Eye Institute at Hopkins, and hone her clinical skills by observing patients in the Vasculitis Center.

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“Cyclophosphamide”

Our newest medication brochure, “Cyclophosphamide“, is now available online at <http://vasculitis.med.jhu.edu> and in hard copy by request.

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Clinic Corner: Please Bear With Us On Thursdays	
<p>Thursday, our busiest day of the week in clinic, is when Drs. Hellmann, Regan, and Stone all evaluate patients on the same day. In addition to our faculty, we also have fellows, residents, and medical students in clinic that day. For the Vasculitis Center Patient Coordinators on Thursdays, there are appointments to schedule, tests to order, consults to arrange, and many other unforeseen tasks. The result is controlled chaos, which Danielle, Judy, and our new Patient Care Coordinator (to be named) strive mightily to maintain.</p> <p>On Thursdays, so that we can devote our full attention to patients who need our attention in clinic, we ask for special forbearance from you. On that day you will find the following message on the Vasculitis Center telephone line:</p>	<p><i>“Due to large number of patients evaluated in our clinic on Thursdays, it is possible that there will be a delay in returning your call. We apologize for any inconvenience that this may cause you. If you are having a medical emergency, please hang up, call 410-955-6070, and ask to speak with the Rheumatologist on call. Non-urgent messages may be left on this answering machine, and we will return your call by the close of clinic on Friday. We appreciate your understanding on our busiest clinic day of the week. Thank you very much.”</i></p> <p>While we are in clinic on Thursdays, let us know immediately about any urgent problems. For non-urgent issues, please understand that we may not return your call until Friday.</p>

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 WE'RE ON THE WEB!

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