

PHYSICIAN **Update**

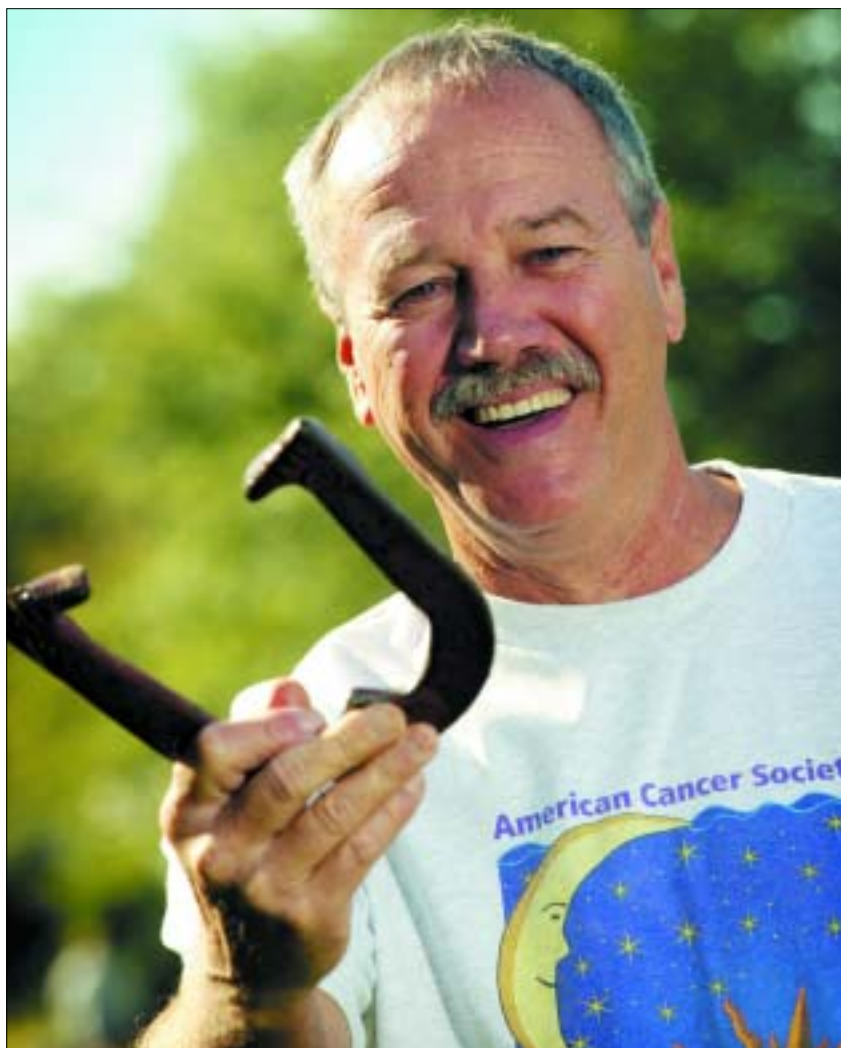
FOR HOPKINS CLINICAL FACULTY AND REFERRING PHYSICIANS

A Melanoma Patient Benefits from a Group Approach

Two summers ago, retired school-bus driver Robert Rinker was doing what he does best, pitching horseshoes, when his wife and daughter noticed a dark, raised area on his back. The 62-year-old Edgewood, Md., man couldn't see it, couldn't touch it, and didn't pay much attention to it until he bumped the spot weeks later and it started to bleed. Then he went to see dermatologist **Mona Mofid**, who removed some of the lesion for examination under a microscope and confirmed his worst fears.

"She called three days later and asked me and my wife to see her in her office," Rinker says. "It was melanoma. I was scared because I knew that cancer moves fast, and I had just read about Ronald Reagan's daughter dying from it. I felt like my life was in Dr. Mofid's hands."

Rinker had good reason to be scared. His melanoma was one of the deepest Mofid had ever seen. And because of the depth of the tumor, there was a strong likelihood that cancerous cells had already spread to his lymph nodes. Rinker would need a sentinel node biopsy, right away, to determine if there had been any metastatic spread. Then he'd need quick consultation and coordination between highly skilled dermatologists, medical oncologists and cancer surgeons to give him his best shot at



Robert Rinker, back pitching horseshoes after receiving collaborative melanoma care at Hopkins.

long-term survival. Patients with Rinker's stage of melanoma have only about a 60 percent chance of living five years.

Luckily for Rinker, Hopkins turned out to be one of the few places in the country where a group of physicians—known collectively as the Melanoma and Cutaneous Oncology Group—get together daily to go over the most complex cases. This collaboration made it easy for Mofid to quickly arrange a biopsy of

Rinker's lymph nodes with a surgeon. When the biopsy came back negative, Mofid then set up an appointment for Rinker with medical oncologist **William Sharfman**. He evaluated the melanoma and then referred Rinker to surgeon **Maurice Nahabedian**, who removed the melanoma. To reduce the chance of any cancer cells to be left behind, Nahabedian left a wide, 2-centimeter margin on each side of the tumor.

Rinker's next stop was with Sharfman again, who recommended Interleukin-2 therapy to further reduce the risk of any cancer spread. Rinker suffered serious side effects, including fatigue and significant weight loss, but today, more than two years after his melanoma was detected, he says he's feeling great. His weight, which had dropped to 150 pounds, is back to 184. He no longer has to take any blood pressure medicine and, best of all, he's back pitching horseshoes.

"Dr. Mofid was my savior," Rinker says. "She was very, very good; she took over everything." But it is the group,

Pulling Zebras Out of the Pack

Dermatopathologist **J. Margaret Moresi** recalls the case: a community physician wanted another look at a suspected melanoma. Looking through her microscope at a tissue sample treated with special histologic stains, Moresi right away saw ambiguous features that made diagnosis difficult. The epidermis wasn't as involved as it usually is in melanoma, and there was no pigment in the cells, as is typical for melanoma. Moresi was leaning toward a diagnosis of benign, but then took one more step. She stained the tissue with a marker that would show an increase in cell division within the dermis, an indication of malignancy. Bingo! She had her answer: "It didn't look like melanoma, but it was."

Terry Barrett, who like other dermatopathologists spends 90 percent of his time evaluating melanoma biopsies, explains that melanomas aren't always clearcut. But a correct diagnosis is critical, he adds, because melanoma can be cured only if it is caught early. "The ones that are difficult to detect are the ones we end up getting here," Barrett says. "It's made us become pretty good at pulling the zebras out of the pack." ☎ 410-955-6467 (ext. 76).

Mofid stresses, that makes the difference for patients like Rinker: "Very few institutions take the top doctors in melanoma and put them in a room together, where they sit around a table and take ownership of a patient." For more information: ☎ 410-955-6467 (ext. 69).

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A New Way to Diagnose Suspicious Thyroid Lesions

A patient feels a lump in the front of his neck and rushes off to his family doctor with fears of thyroid cancer. Relax, his physician says, such nodules are common and in 9 out of 10 cases a fine needle aspiration (FNA) proves them benign. But, as it turns out, this patient's case isn't so clearcut. When cells are retrieved from his neck with the small needle used for the FNA and examined under a microscope, whether or not they are malignant still isn't obvious. In most such instances, doctors will proceed on the side of caution. They'll either send the patient to the operating room for a partial removal of the thyroid so a tissue biopsy can be performed, or they'll advise that the entire gland be removed immediately, since 30 percent to 40 percent of suspicious thyroid lesions eventually prove malignant.

In other words, says endocrine surgeon **Martha Zeiger**, in those cases in which an FNA can't confirm whether a thyroid lesion is malignant, we have two less-than-perfect options—take out half the thyroid, and if it comes back cancerous, bring the patient back for a second

surgery to remove the rest of the gland. Or take the whole thing out, when that may not even have been necessary.

So concerned has Zeiger been about these harder-to-diagnose patients that for the past eight years she's been in the lab searching for molecular markers that can clearly say benign or malignant without the need for a surgical biopsy. Using gene expression techniques, in 1999 she found telomerase—which had been shown to be active, or “expressed,” in breast and prostate cancers—to be 93 percent accurate in picking up some, but not all, cancers in suspicious thyroid lesions.

Now Zeiger's using another marker, a mutation of the BRAF gene, recently shown by Hopkins otolaryngologist **David Sidransky** to be present in two-thirds of papillary thyroid cancers, the most

common type of malignancy in this gland and most commonly found in women (*Journal of the National Cancer*



Surgeon **Martha Zeiger** makes sure the thyroid gland (inset) is removed only when it's absolutely necessary.

Institute, April 16, 2003).

“From the patient's point of view, finding the marker can be considered a major step forward, because it allows us to avoid putting them through unnecessary surgery,” points out Zeiger, who's developed a clinical study using the identifying trait. “Almost 100 percent of the time, if someone has the mutation we can be certain the person has a cancer. In that case, I would take out the whole thyroid in one operation.”

For more information or patient referrals: ☎ 410-955-6467 (ext 70).

AUTOIMMUNE DISEASE

Dramatic Results in Managing Lupus

What causes lupus remains a mystery. What's clear is the extent of the damage the disease can wreak on the human body as the immune system mercilessly attacks its own joints, kidneys, heart, lungs, brain, blood and skin.

“Living with long-term lupus is devastating,” rheumatologist **Michele Petri** states categorically. “In about half our patients, the disease has permanently damaged one or more organ systems despite all the help we can give these people with the most current therapies.” These consist of low doses of the cancer drug cyclophosphamide taken once a month for six months and then once every three months for two years. Sadly, only about 25 percent of lupus patients respond. And for some of them, the cure is worse than the disease. Long-term exposure to cyclophosphamide causes horrendous bladder and ovarian problems and puts a person at high risk of developing cancer.

For awhile though, Petri had seen a ray of hope for her patients. Hopkins researchers, looking for better treat-



Michele Petri with Paula King, the first patient to receive the new high-dose, short-term cyclophosphamide.

ment for autoimmune diseases, had produced astonishing turnarounds with severe aplastic anemia, an even more-lethal condition, and also in some cases of lupus. The new approach involved using a shorter, but higher-dose regimen of cyclophosphamide. “The idea,” Petri explains, “is to blast the lupus once and wipe out the abnormal immune system and then allow the

body to relearn and function normally without further therapy.”

A couple of years ago, Petri, with oncologists **Robert Brodsky** and **Richard Jones**, conducted a small clinical trial with the new method on a group of lupus patients who have significant organ failure and who had failed to improve with conventional therapies. Now, the numbers are in, and once

again, the new approach has yielded dramatic results. Thirty percent of the patients in the trial went into a long-term remission. Today, almost three years after the study, there is no evidence of the disease in their bodies. About 50 percent had a partial response and continue to take lower doses of previously ineffective immune-suppressing drugs. “That's a huge advance,” Petri says. “Even when the disease came back, it didn't come back full force.”

Also, because the therapy preserves stem cells while blasting the abnormal immune cells (creating a reborn immune system) a bone marrow transplant is not necessary to replenish stem cells. The high-dose therapy knocks the white blood count down to zero for about 10 days, so patients come into the hospital daily to be checked for infections. Another benefit—the high-dose treatment is less likely to cause infertility, a side effect of the long-term, low-dose treatment. “Two of these patients have had a successful pregnancies,” Petri says, “something they were unable to do before.”

For more information or patient referrals: ☎ 410-955-6467 (ext 71).

Going After Hard-to-Get Spinal Tumors

This spinal tumor couldn't have been located in a more inaccessible location—the uppermost region of the cervical spine near the base of the skull. To get to it, surgeons once would have used a limited approach through the mouth or neck, which would have let them remove only part of the mass.

“We'd take it out as best we could and rely on other treatments like radiation therapy to take care of any tumor we left behind,” says neurosurgeon **Ziya Gokaslan**. “Historically, these patients did rather poorly.”

But Gokaslan, with head and neck surgeon **Anthony Tufaro**, has found a way, right through the jaw, to access these hard-to-get tumors and give new hope to patients. In the first part of this com-

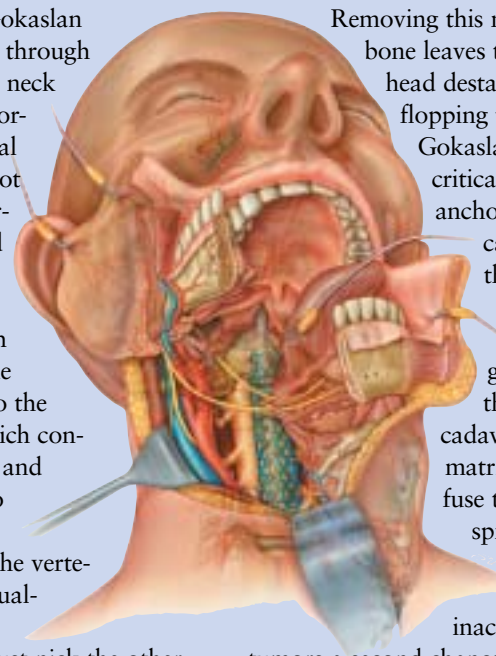


Neurosurgeon Ziya Gokaslan developed the technique he uses to remove tumors on the cervical spine (see illustration by Ian Suk).

plex surgery, Gokaslan and Tufaro cut through the back of the neck to remove tumor-engulfed cervical bone, careful not to injure important nerves and the vertebral arteries. These arteries on each side of the spine supply blood to the brain stem, which controls breathing and heart rate. Also inundated by tumor, one of the vertebral arteries usually has to be removed. But just nick the other one and the patient will die in the operating room.

“We would not take the artery within the tumor itself unless we were 100 percent certain the other vertebral artery was fine,” Gokaslan says.

Next, the surgeons split the jaw to access and remove the rest of the tumor in front of the spine. But that's only half the battle.



Removing this much cervical bone leaves the patient's head destabilized, literally flopping to the side.

Gokaslan solves that critical problem by anchoring a cylindrical steel cage to the remaining bone above and below the gap. The cage is then filled with a cadaveric bone matrix that helps fuse this new cervical spine, giving

patients with previously inaccessible spinal tumors a second chance they hadn't expected.

“Patients sometimes have difficulty with swallowing and tongue function, but that usually recovers over time and they end up having a good quality of life,” says Gokaslan, who specializes in what he calls the most complex spinal tumor cases. “And we've removed a tumor that was previously unremovable.” For more information or patient referrals: 410-955-6467 (ext. 72).

HEMATOLOGY

An Answer for Adult Sickle Cell Patients

Ask hematologist **Sophie Lanzkron** to name the milestones in treating sickle cell disease, and she'll shoot back the names **Sam Charache** and **George Dover**. In the early 1980s, the two Hopkins hematologists led trials of hydroxyurea, which dramatically decreased the number of excruciatingly painful “crises” patients experience when their disfigured red blood cells (they look sickle-shaped) stick together and clog vessels, starving tissues of needed oxygen. With the new drug, patients' crises declined by 60 percent, and the life-expectancy of sickle cell patients increased from the teens to the mid-40s. But with that step forward, what was once solely a children's disease became a disease for adults, too. And, curiously, that presented another challenge—how to take care of them.

“There are programs for kids, but nothing for adults,” Lanzkron says. “It's a population that has been neglected.”

No more. Lanzkron has established the Johns Hopkins Sickle Cell Center for

Adults, one of only a few such centers in the country, where physicians in the Mid-Atlantic region refer patients for help in decreasing their painful crises. Regimens must be carefully calibrated to each patient's disease level, no easy task.

“A lot of community physicians don't have the resources to monitor patients' labs every two weeks to make sure they're on the correct dose,” Lanzkron says. “That's one of the services we're able to offer.”

The center also offers a specialized blood bank for adult patients who need constant transfusions to keep life-threatening infections and such complications as stroke and blindness at bay. Because one-



Hematologist Sophie Lanzkron helps patients like Joseph Dredden better manage their crises.

quarter of sickle cell patients develop antibodies against donor blood, “chronic transfusion therapy” is not without risks. Patients must infuse themselves daily

with medications like Desferal, for example, to remove accumulating iron in their blood from the numerous transfusions. As part of an academic medical center, Lanzkron can investigate hemoglobin-based oxygen carriers that reduce the need for transfused blood. Those artificial blood-type products also prevent sickle cell patients from developing antibodies against them. Finally, Lanzkron is studying a new agent that may be able to prevent crises altogether.

“If you want to offer a top-notch treatment for a particular group of patients,” Lanzkron says,

“you need to be on the cutting edge when it comes to available therapies.” For more information or patient referrals: 410-955-6467 (ext. 73).

Sturge-Weber: A Devastating Disease Beneath the Skin

As pediatric dermatologist **Bernard Cohen** examines the purplish blotch on his 3-year-old patient's face, it's not the so-called port wine stain that concerns him the most. He knows that the discoloration covering her left eye, forehead and scalp follows the first branch of the trigeminal nerve beneath the skin. That means his patient could have Sturge-Weber syndrome, or SWS, which begins in utero as a spider-like tangle of abnormal blood vessels in the tissues surrounding the brain. This patient is not only afflicted with a facial disorder—she may be facing glaucoma, seizures, strokes and developmental delays, too. “What appears to be in the skin only can

sometimes lead to a major disability, socially and medically,” Cohen says.

Using the latest laser therapies, Cohen says he is able to eliminate up to 75 percent of the port wine stains in the majority of his patients. Patients who wear the marker for SWS he refers to the Johns Hopkins Sturge-Weber Syndrome Center, a new option for patients who in the past have had to shuttle between specialists at several institutions for treatment.

“There hasn't been one place patients could go to get a multidisciplinary assessment by experienced people,” says pediatric neurologist **Anne Comi**, referring to



Dermatologist Bernard Cohen with a young Sturge-Weber patient.

the endocrinologists, ophthalmologists, neurologists and psychiatrists at the center.

The center's approach, Cohen stresses, hinges on early diagnosis. Infants are screened at birth for signs of glaucoma. MR perfusion imaging is used to spot brain areas at high risk of ischemic damage, and EEG to predict who'll have severe disease.

“If you delay treatment, you get thickening of the skin and soft-tissue changes that make it more difficult to treat,” Cohen says. “Early treatment can prevent those complications.” For more information or patient referrals: ☎ 410-955-6467 (ext. 74).

PEDIATRICS

Week by Week, Overweight Children Learn Appetite Control

Medical assistant **Kim Ladson** worked at Johns Hopkins, but she didn't have a clue that the medical center had a comprehensive weight management clinic for children. Hopkins was about cutting edge medicine, she figured, the latest surgical techniques—not how to keep excess pounds off. But that's exactly what she wanted for her 11-year-old daughter, **Andrea**, who was making little gains with dieting alone. “I thought it would be really great for Andrea,” Kim says. “We might actually see some results.”

First, Andrea had a physical with pediatric gastroenterologist

Ann Scheimann, who looked for any health problems related to obesity, like high blood pressure and joint problems. Scheimann also searched for underlying hormonal conditions contributing to Andrea's overeating. Finding none, she sent Andrea to nutritionist **Merel Schollnberger**, who

had her fill out an assessment of her eating habits. Does she eat with her family, in her room, in front of the TV? Then she asked Andrea to write down everything she eats and drinks for



Andrea Ladson, with pediatric gastroenterologist Ann Scheimann, found there's more to losing pounds than dieting.

three days. “It's tedious,” Schollnberger says, “but the first step in any behavior change is to become aware of what your habits are.”

Andrea also met with a

psychologist, who talked to her about the taunting she was being subjected to in 5th grade. Overweight kids tend to feel isolated, which can lead to depression, which can lead to even more overeating. She also introduced Andrea to her weight management group, kids just like her. “In a peer group that isn't going to tease them, kids become more open,” Schollnberger says.

Scheimann tends to put morbidly obese patients on a strict high-protein, low-fat diet. But

overweight patients like Andrea go on a “low glycemic” diet that avoids foods that increase blood-sugar levels and, consequently, craving. It's a gradual weight-loss approach in which kids lose 1 to 2 pounds a week. Andrea lost 20 pounds in the first five months. “If we look for them to lose an extreme amount of weight in a short period of time,” says Schollnberger, “they'll quickly go back to their old habits.”

“Andrea feels a lot better about herself,” adds her mother, “and that's what makes me happy.” For more information or patient referrals: ☎ 410-955-6467 (ext. 75).

Johns Hopkins PHYSICIAN Update

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