clevelandclinicmagazine
Spring / 2006

Face:

The Final Frontier of Transplantation

Protecting Research Volunteers | Children and Stroke | A Special Look at Cancer

INTERCONTINENTAL.
HOTEL CLEVELAND

Sophisticated.

The finest traditions of international service and elegance live at the InterContinental Hotel Cleveland.

Elegant guest rooms, high-tech amenities and easy access to medical facilities make this world-class hotel your choice for the perfect accommodations in Cleveland.

Classics, the hotel's AAA Five-Diamond restaurant, offers the most sophisticated dining experience between New York and Chicago.

For reservations, call
1.877.707.8999

clevelandclinicmagazine
SPRING / 2006

Volume3Issue1

Questions, comments or requests for more information:

E-mail:
clevelandclinicmagazine@ccf.org

Mail:
Managing Editor
Cleveland Clinic Magazine
Cleveland Clinic/W14
9500 Euclid Avenue
Cleveland, OH 44195

Phone:
216.445.4908

Web:
Please visit our Web site at
clevelandclinic.org/clevelandclinicmagazine

Cleveland Clinic

COVER STORY

Face: The Final Frontier of Transplantation 20

Some only go out at night. Others never leave their homes. For people with severe facial disfigurement, the emotional and personal pain can be debilitating. "The face is the most visible part of you," says Maria Siemionow, M.D., Ph.D., D.Sc. Unsatisfied with the limited help currently available to restore facial appearance and function, Dr. Siemionow plans on performing a bold new procedure: The world's first full facial transplant.

Features

First, Do No Harm 10

Research is big at Cleveland Clinic. But before any research can begin, it must first be approved by the Clinic's Institutional Review Board. This 13-member panel is charged with ensuring that people who volunteer for scientific research are respected, informed and protected throughout the research process. Using a rigorous review process, the Institutional Review Board works to protect research participants and, in doing so, protects us all.

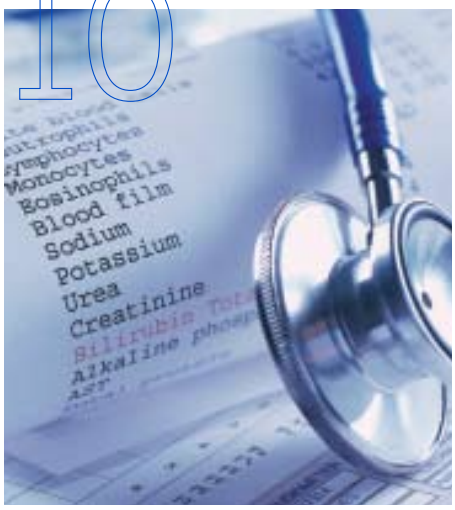
Opening Pandora's Box: A Special Look at Cancer 16

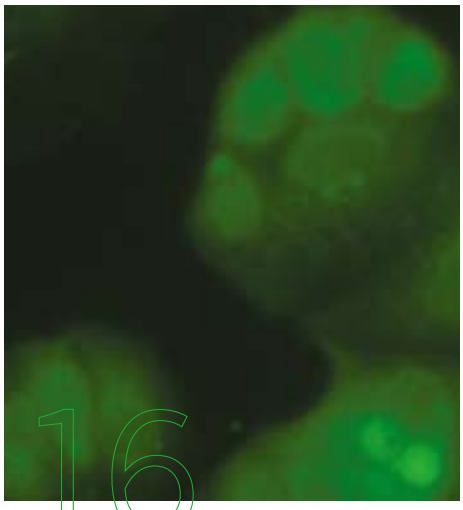
According to mythology, when Pandora opened the box she released into the world innumerable plagues. The box, however, also contained one other element: hope.

Researchers in Cleveland Clinic's new Genomic Medicine Institute are working night and day searching for clues into the causes of cancer – research that will one day lead to new treatments for millions of people with this disease.

Never Too Young: Strokes can happen at any age ... even before birth 24

Adults are not the only ones who can suffer a stroke: children get them, too. In fact, pediatric stroke affects more than six in every 100,000 children yearly, nearly twice the number of children affected by brain tumors. Cleveland Clinic pediatric neurologist Neil Friedman, M.B., Ch.B., says that pediatric stroke is "under-recognized and under-diagnosed," and he wants that to change.





In This Issue

The First Word 3
Care Without Boundaries

The Medicine Chest
The Future of Throat Surgery 4
Seeing Through Young Eyes 5
A Soft Model for Hard Planning 6
9-volt Fix 6
New Direction in Detecting Lung Disease 7

On the Web
Diagnosis Challenge 8
The Patient with Aches and Changes
Physicians see hundreds of patients a year, with every day bringing new challenges. In this section, we offer our readers the chance to follow a physician through the diagnostic process. What diagnosis will you make?

Readers' Poll Results 8
Read our our organ donation poll results.

Readers' Poll 9
Tell us what you think about whole facial tissue transplantation.

Philanthropia
Sydell Miller: 30
Giving Today for Better Healthcare Tomorrow

Michael and Dianne Bienes: 30
A Good Philanthropic Investment

R.E. and Beverly Allen: 31
In Loving Memory and Good Health

Ralph and Luci Schey: 32
Keeping a Promise

Ask the Experts 34
Reducing More Than Weight
Obesity is a national healthcare crisis, responsible for many serious medical conditions. For severely overweight people, weight loss surgery can improve their health and change their life. Bariatric surgeon Philip Schauer, M.D., explains.

Florida Focus 36
A Small Approach to a Big Problem
Approximately 600,000 women undergo hysterectomies annually. While most women considering a hysterectomy are candidates for a laparoscopic approach, many surgeons still perform the standard surgical procedure. Gynecologic surgeons at Cleveland Clinic Florida are using the laparoscopic approach in almost 97 percent of cases. The benefit to patients: smaller incisions, lower risk of post-operative infection and a significantly shorter and less painful recovery time.

On the Horizon
Bringing Innovation Down to Earth 38
Taking Pain Relief to Heart 39
Removing Sox to Prevent Disease 40
The Flow Must Go On 40
Old Tropical Infection Drug is New Anti-Tumor Hope 41

Living Healthy 42
Managing Multiple Medications
Most of us don't think that taking more than one medication or repeating a medication can be a health hazard. But as more and more medications are prescribed for people – particularly older adults – the risks associated with "polypharmacy" increase. Learn how you can prevent a bad mix of medications.

My Story 43
The Double Switch
A blog by Neal Freeland
"Amelia's heart is like a wind-up toy. At her birth, we were afraid the whole thing, once on its own and free of the umbilical cord's steady guidance, would spin too rapidly and blow apart. Fortunately, that didn't happen ... Now, the question is 'how fast is it winding down?' ... the answer seems to be 'fairly quickly' ... .

To read more stories from this issue, go to our Web site: clevelandclinic.org/clevelandclinicmagazine.

CARE WITHOUT BOUNDARIES

Medical centers are typically organized around professional divisions, such as surgery and medicine. These divisions are holdovers from the early days of the medical profession. They represent a physician-focused approach that is no longer in tune with emerging medical practice.

At Cleveland Clinic, we are changing the way we deliver patient care by bringing multiple specialties together into patient-focused institutes. These institutes are based on organ and disease systems. They combine services in a common location and share a common leadership. More than a new name for old departments, institutes are an efficient and more effective approach to patient care.

The advantages of institutes are clear. By bringing services together under one roof, patients have the advantage of remaining in one location for all of their care, including consults, tests and imaging.

Institutes also promote a multidisciplinary approach to medicine. They break down professional divisions and make it easier for medical doctors, surgeons and other specialists to work together. They promote the intellectual cross-pollination that leads to innovation and better patient care.

As the site of clinical research, institutes make it possible for scientific breakthroughs to be quickly and safely translated into new treatments and cures. For our educational programs, they permit greater collaboration by exposing residents and fellows to the full medical and surgical expertise of their specialty in one area.

Examples of these types of organ and disease-based institutes can be found throughout Cleveland Clinic. They include the:

Heart and Vascular Institute
Glickman Urological Institute
Cole Eye Institute
Head and Neck Institute
Neurological Institute

Each institute combines many departments. For example, the Neurological Institute comprises Neurology, Neurosurgery, Neuroradiology, and Psychiatry and Psychology. The Heart and Vascular Institute includes Cardiovascular Medicine, Thoracic and Cardiovascular Surgery, Vascular Surgery, Vascular Medicine, Cardiac Anesthesia, Cardiac Radiology and Cardiac Pathology. The Urological Institute combines Urology, Nephrology and Dialysis.

Cleveland Clinic has a distinct advantage in the development of institutes. Our group practice model of medicine has always encouraged physician teamwork and collaboration. The institutes model takes this collaborative effort to a whole new level. We also are a leader in the use of the electronic medical record. Through the EMR, all our physicians have fast, confidential access to the data they need to share advice and provide the most effective care for every patient.

We see this new approach to the organization of patient care as the wave of the future. It may challenge some existing professional boundaries, but we welcome change when change improves care. These institutes will succeed because they are arranged for the health and convenience of patients. They put the patient first. And that is what Cleveland Clinic is all about.

Delos M. Cosgrove, M.D.
CEO and President

The Future of Throat Surgery

Using lasers to remove tumors and other growths from the throat has always been a bit of a top-down affair. Surgeons peer down the patient's throat to gain direct sight of the target tissue, then vaporize it in segments with a fixed external laser attached to an operating microscope.

But now, with the help of a CO_2 laser fiber and a surgical robot, doctors at Cleveland Clinic have introduced a more flexible approach to throat surgery, one that allows tumors to be viewed and removed quicker and with greater precision.

Developed by a research team from the Massachusetts Institute of Technology, the laser energy is delivered from the end of a flexible, spaghetti-thin fiber that can be positioned above, beneath or next to the target tissue. Moving the fiber into precise position is a surgical robot, called Da Vinci, more commonly used in heart surgery. Providing surgeons with an unequalled 3-D close-up of the operating area are twin mini-cameras – an extra pair of super-powered eyes set at the end of fiberoptic cables.

"The paired cameras, combined with the flexible laser, provide an amazing depth of field," says Marshall Strome, M.D., an otolaryngologist and Chairman of the Cleveland Clinic's Head and Neck Institute. "They enable me to see the tumor better than ever before and, when used in combination with the flexible laser fiber, also allow more strategic incisions, initially speeding the overall operation."

During the procedure, Dr. Strome works from a nearby booth, watching the video feed and manipulating hand controls that get translated into the delicate movements of the twin robot arms that move laser, lights and cameras.

"This is the future of throat surgery," he says. "As the lasers and robots continue to evolve, I see them being used for a full range of procedures, whether it's a tumor of the vocal cords, tongue or wall of the throat."

While robotic and laser surgery currently requires the surgeon and patient be in the same room, Dr. Strome envisions a day when such surgeries will be performed remotely, from across town or from across the globe.

Seeing Through Young Eyes

The ReSTOR lens helps reduce dependence on reading glasses or bifocals after cataract surgery. A series of rings etched into the lens' surface collects and distributes light in such a way that wearers get both distance and near vision at the same time. *Image courtesy of Alcon, Inc.*

Almost half of people over age 65 have cataracts, clouding of the eye's natural lens that eventually leads to vision impairment or loss. Many undergo cataract surgery, which involves removing clouded lenses and replacing them with intraocular implants made of high-density acrylic. The vast majority of people who undergo the procedure are implanted with monofocal lenses that give them distant vision in both eyes or distant vision in one eye and near vision in the other. Following surgery, many need to use reading glasses or bifocals for near vision.

The AcrySof ReSTOR intraocular lens, approved by the United States Food and Drug Administration (FDA) in March 2005, significantly reduces the need for glasses for some people after surgery. "It's a bifocal lens, which means it lets you see both near and far," explains Cleveland Clinic Cole Eye Institute surgeon Allen S. Roth, M.D.

Noting that the FDA study showed that 80 percent of the patients who had received the lens had a return to visual acuity of 20/25, he adds, "It's like having young eyes again."

Through a process called apodization, the lens contains a series of concentric rings that resemble a bull's-eye. The rings send incoming light to focal points responsible for near vision and distant vision, providing clear vision up close and from a distance at the same time.

ReSTOR isn't for everyone. People with astigmatism, which is curvature of the cornea, aren't candidates, and it generally isn't for people who only have a cataract in one eye.

A Soft Model for Hard Planning

The image of a skull pointed Angela Noecker toward a way to help physicians plan more complex surgery and educate patients.

While creating a skull model for plastic surgeon Risal Djohan, M.D., Noecker, a Senior Research Engineer with the Department of Biomedical Engineering's Medical Device Innovations Group, started to mull the possibility of developing soft tissue models for certain cases. "I knew it would be a little extra work to do the soft tissue but thought it might help surgeons prepare for more precise or complex cases," she says.

Soft tissue models start just as hard tissue models do – with commercially available software, a computer and the means to manufacture a model. Noecker develops 3-D digital models from multiple computed tomography (CT) scans and then programs a stereolithography machine to create rigid models of soft tissue, such as skin and muscle, from the scans. In the case of a facial reconstruction patient, the soft tissue might be the skin and tissue around an eye socket and the upper cheek area, for example.

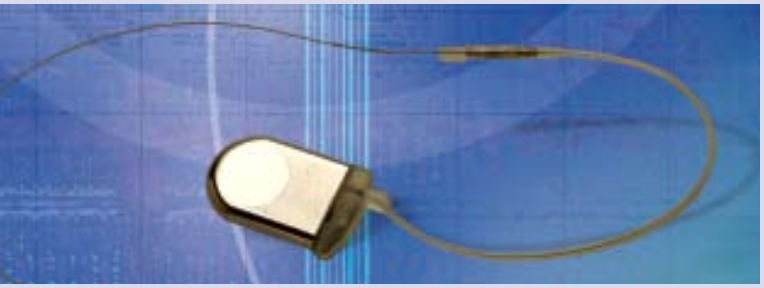
The rigid models, which can be built within a matter of hours, are given then to Ji-Feng Chen, Senior Principal Research Engineer in the Biomedical Engineering polymer laboratory. Chen's lab uses the models to create molds, into which liquid silicone or polyurethane is poured. After the material solidifies, the halves of the mold are separated and surgeons have a pliable model of the patient's head, which shows precisely the amount of soft tissue that is required prior to surgery.

The models of hard and soft tissue taken together create an exact representation of what the patient looks like. A similar set of models is created by mirroring the opposite (uninjured) side of the patient's face to create a representation of the desired outcome. Physicians can then use the models to determine exactly what work needs to be done and what methods may not work well, without needing to test them out on the patient. The first applications of this new technique were used by Dr. Djohan and his team for facial reconstructions.

"Not only does the model help us plan our surgery, but sometimes there are choices that need to be made by the patient, or we have to explain the need for multiple operations," Dr. Djohan says. "3-D models demonstrate the procedures much better than 2-D images. Patients can understand what's going to happen better if they have a model they can hold in their hands rather than by looking at a series of X-ray films."

Above: Angela Noecker

9-volt Fix



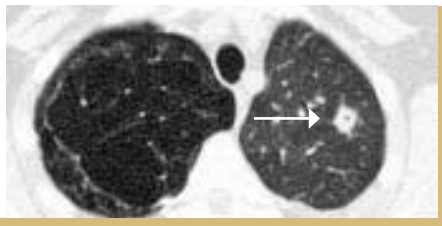
The OsteoGen-M uses electrical impulses to stimulate bone growth in patients with hard-to-heal ankle fractures. *Image courtesy of EBI Medical, Inc.*

When most patients undergo ankle surgery to fuse fractured bones, the bones typically heal without incident. But in a small percentage of patients with poor bone health, the fracture doesn't heal, leading to a potentially chronic and debilitating condition.

A new procedure using electrical impulses to stimulate bone growth is giving those 5 percent to 10 percent of patients for whom ankle surgery is not successful the opportunity to return to an active life.

The implantable bone growth stimulator is the latest – and, to date, most highly successful – method of stimulating bone growth and promoting healing.

New Direction
in Detecting Lung Disease

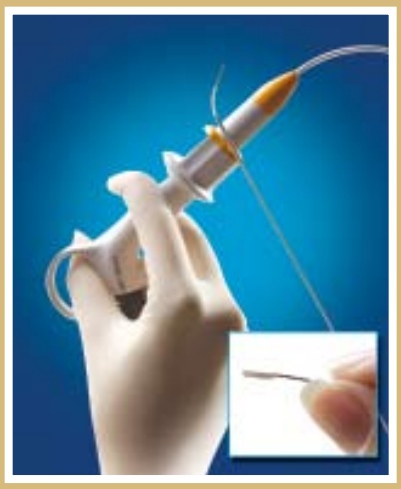


Global positioning system (GPS) technology can do wonders when you're driving in a foreign city. Lost while maneuvering the side streets? No problem. Just punch a few buttons on the dashboard and instantly you have a map of where you are as well as guidance on the best way to get where you're going.

Similarly, doctors at Cleveland Clinic are pioneering the use of a GPS-like tracking system that helps them navigate the complicated roadway of branches inside people's lungs. Using a 3-D "map" of a patient's lungs generated by computed tomography (CT) scans to guide them, doctors can "drive" a probe that has been inserted into the lungs via a bronchoscope. The system helps guide biopsy instruments toward small lesions in the lung – often seen as "dark spots" on chest X-rays – and enables doctors to more reliably diagnose these tumors and plan for treatment before the tumors have a chance to grow and become more problematic.

"What's exciting about this is that, previously, using just CT scan imagery, we could see the area where we wanted to biopsy, but the bronchoscope could see out to only a couple of branches of the lung, so we were driving blind the rest of the way," says Thomas Gildea, M.D., Medical Director of Cleveland Clinic's Center for Major Airway Diseases. "Now we can use the CT scan and the navigation technology to guide the biopsy instruments to all the parts of the lung."

Using routine bronchoscopy, Dr. Gildea says, doctors can accurately diagnose only about 14 percent of lesions smaller than two centimeters in diameter located in the outer portions of the lung. Today, using the GPS-like technology, three-quarters of all lesions can be sampled. "Because of early detection, patients with small abnormalities that prove to be cancer have a much better survival rate. The system also is useful to delineate a benign from a malignant lesion in some patients," he says.



Another benefit of this new technology is patient safety. Inserting a bronchoscope through the nose or mouth to biopsy a suspected spot on a lung is much less of a risk than "going in through the chest wall to perform a biopsy," Dr. Gildea says. "Patients with advanced lung disease or other medical problems can avoid the risk of other more invasive biopsy techniques or surgery."

Dr. Gildea believes this procedure will change lung-associated clinical care, because doctors now have the opportunity to proactively treat smaller lesions instead of just monitoring them for change.

Above: CT scan of chest showing the type of lesion (arrow) sampled using electromagnetic navigation.

Left: GPS-like probe and its tip (inset), which can be steered through the complex of bronchial branches to sample small lesions in the lung. *Images courtesy of superDimension, Ltd.*

The stimulator resembles a flattened 9-volt battery pack that is implanted in the patient's leg. A wire attached to the stimulator sends electrical impulses to the fracture, right between the two bone surfaces.

"All bone growth works off positive and negative charges that open up the cellular gates, allowing molecules to heal bone," explains Brian Donley, M.D., Vice Chairman of Orthopaedic Surgery. "The stimulator boosts the natural biochemical polarity that occurs and improves the body's ability to produce more bone."

Those at risk of poor bone health include smokers, diabetics, some elderly patients and those with a history of fractures that don't heal properly. There are no real risks associated with the device and patients don't feel any electrical impulses. "It can cause some discomfort because it is a large battery under the skin," says Dr. Donley, adding that it may not be a good option for some patients, including those who are very thin.

Although several different types of bone-growth stimulators currently are available, this new version is the most appealing. Once the device is implanted, the patient can forget about it until the battery runs out. When the healing is complete, typically in six months, the device is removed in an outpatient surgical procedure.

Diagnosis Challenge

Physicians are often called upon to diagnose a wide range of symptoms and conditions. In this section, we offer our readers the chance to follow a physician through the diagnostic process. What diagnosis would you make?

The Patient with Aches and Changes

Michelle* adjusted the thermostat in her home, cranking up the heat to 75 degrees. Settling into her favorite chair and putting her feet up – her legs ached lately – she closed her eyes and exhaled, forcing a day's worth of deadlines and corporate stress from her worn-out body. She reached for her favorite bottle of vanilla moisturizer and slathered a helping of it on her dry hands.

"Why is it so cold in here?" she remarked flatly.

Her husband, Tom, didn't hear her complaint over the drone of the six o'clock news. Lately he was used to his wife's moodiness. Michelle, even at 55, was still driven – he loved that about her. She was responsible for luring in a number of high-profile clients at work this year, and he blamed her distractedness and mood swings on her demanding schedule.

Michelle called out to Tom, "Let's just have salads tonight." She had gained 10 pounds in the last three months; strange, because her eating habits hadn't changed. She wondered if a change in her metabolism might be responsible. She felt tired. Even her boss had commented at her last review that she seemed worn out – not the spunky, energetic marketing guru her co-workers knew.

Over dinner, Tom convinced Michelle to see a doctor about her symptoms. He was worried that she was not taking care of herself.

The Office Visit

Cleveland Clinic endocrinologist Christian Nasr, M.D., listened while Michelle described her lifestyle. He sensed that the seasoned career woman had always put her health on hold or at least used her busy schedule as an excuse for fatigue and moodiness. Michelle told him she was experiencing the onset of menopause, and she complained a bit about her dry skin, remarking that she was getting old.

Christian Nasr, M.D.

Dr. Nasr noted her concerns and proceeded with some routine questions. Michelle told him that her father's side of the family has a history of heart disease, and that her mother has high cholesterol. Dr. Nasr noticed that Michelle did not remove her jacket while he interviewed her. After collecting more information on Michelle's health concerns and family medical history, Dr. Nasr conducted a thorough physical examination. He recorded her weight gain and dry skin patches. He did not notice swelling near her thyroid gland. He ordered a cholesterol test and took her blood pressure. Her cholesterol was a bit high: 250. Her blood pressure was above normal.

As Michelle grew more comfortable with Dr. Nasr, she confided that she felt depressed. She admitted that her mood swings, fatigue and unmotivated behavior were not like her.

Readers' Poll Results

The Gift of Life: Organ Donation

In our last issue, we invited readers to tell us their thoughts on organ donation. Here is a sampling of what they had to say in our informal poll:

91% are willing to donate an organ

54% are registered organ donors

14% have donated an organ

To increase organ donation:

72% plan on registering to be an organ donor

45% said we should have more programs similar to Ohio's organ-matching program

24% liked the idea of offering incentives of some kind

19% said that research into new technologies that sidestep organ donation is more important than increasing donations

Learn the facts about organ donation and register with the Ohio Donor Registry by visiting LifeBanc at **lifebanc.org.**

Many of the symptoms she described could be overlooked, but the combination of Michelle's physical and psychological conditions sparked concern. Based on the physical examination and discussion, Dr. Nasr formed a few theories:

Depression – Loss of energy, fatigue, moodiness and a feeling of worthlessness are a few signs of depression. A severe or prolonged depression that interferes with the ability to function, feel pleasure or maintain interest is more than a "case of the blues."

Stress – Stress is difficult to define, as each individual's threshold for dealing with challenging situations varies. If not managed, stress can cause weight gain, weight loss, fatigue, insomnia, high blood pressure and even lead to serious medical problems.

Hypothyroidism – When the thyroid does not produce enough hormones, it upsets the balance of chemical reactions in the body. Symptoms include weight gain, fatigue, depression, cold hands and feet, dry skin and menstrual dysfunction.

Menopause – Menopause affects women at different ages – as early as 35 and into the 50s. Signs include irregular menstrual periods, changes in appearance (weight gain or weight loss), emotional changes (irritability and fatigue), sleep disturbances and hot flashes or heat intolerance, which can be followed by feeling chilled.

Dr. Nasr's next step was to order a biochemical test to measure Michelle's thyroid stimulating hormone (TSH) level, even though she did not have a goiter (swelling at the neck), which is an obvious visible sign of a thyroid disorder.

Continuing with his assessment, Dr. Nasr considered depression. Weight gain and fatigue were certainly indications. Still, this would not explain Michelle's achy body and tendency to feel cold.

He ruled out stress. Although Michelle had blamed her fatigue and moodiness on her work culture, he thought her symptoms indicated more than the "office blues." Her high blood pressure could indicate more serious health problems.

Michelle exhibited some symptoms of hypothyroidism, but her TSH level measured 5.9, which is just above normal.

Michelle certainly displayed symptoms associated with menopause and basic aging. She hadn't had a menstrual period in months. There was no denying the fact that Michelle was going through menopause, but it didn't explain Michelle's high cholesterol and high blood pressure.

What could be the cause of Michelle's condition?

For Dr. Nasr's diagnosis, go to our Web site at **clevelandclinic.org/clevelandclinicmagazine**.

You can also send us an e-mail at **clevelandclinicmagazine@ccf.org**, and we will e-mail you the diagnosis.

** The patient and history presented in "Diagnosis Challenge" are fictional.*

Take Our New Readers' Poll

Beyond Skin and Muscle:
Face Transplantation

In "Face: The Final Frontier of Transplantation," we discuss the issues surrounding whole facial tissue transplantation (see story, pages 20-23).

Tell us what you think in our new Readers' Poll "Beyond Skin and Muscle: Face Transplantation" at clevelandclinic.org/clevelandclinicmagazine.

Choose Your Health News!

Cleveland Clinic now offers you three ways to get the latest health and medical information from the Web:

Hear
it with our new podcasts at **clevelandclinic.org/podcast.**

See
it on our new video podcasts at **clevelandclinic.org/healthedge.**

Read
it every month in our free Health Extra e-newsletter. To sign up, go to **clevelandclinic.org/healthextra.**

First, Do No Harm

Using a rigorous review process, the Institutional Review Board works to protect research participants and, in doing so, protects us all.

Late in 2004, Cleveland Clinic became the first medical institution in the world to officially give the go-ahead to a procedure that was once merely a Hollywood special-effects fantasy: a complete human facial transplant. (See article, page 20.)

That approval was granted by Cleveland Clinic's Institutional Review Board (IRB), a 13-member panel that serves as gatekeeper and watchdog over all human research performed at the institution. It took the IRB 10 months of discussion and the counsel of a host of specialists before Maria Siemionow, M.D., Ph.D., D.Sc., Director of Plastic Surgery Research, was given the green light to begin screening potential candidates for a face transplant. Typical approval for a research study is between two and four weeks.

Before IRB approval was granted, every element involved in the procedure – from determining the criteria for the recipient and donor, and identifying the risks, including the impact on the donor family; to designing the consent forms – was structured to adhere to the stringent research protections of the IRB-review process.

"Our role in the review is to ask as many questions as we can," says Alan E. Lichtin, M.D., Chairman of the IRB and a physician in the Department of Hematology and Medical Oncology. "Our goal is always research subject protection. Human progress will not occur unless there are people who want to come forward and, through the goodness of their heart, want to participate in research. People won't do that if they feel unsafe or if they feel their rights will be violated."

The IRB's responsibility is to make sure that people who volunteer are respected, informed and protected throughout the research process. "If risks are involved, it's the board's job to ensure that those risks are minimized through study procedures and then make sure the research participants are fully informed of all the risks, benefits and possible alternatives to the study," says IRB member Linda Lewicki, R.N., Ph.D. "Our review is to protect the research participants. Their safety and welfare are paramount."

The IRB's charge becomes an even greater challenge as new medical advances bring procedures that were once the realm of science fiction closer to reality.

"As technology continues to grow, you're going to have more ethical dilemmas in hospitals," says Katrina Bramstedt, Ph.D., a member of the Department of Bioethics. Dr. Bramstedt advised the IRB on bioethical issues pertaining to Dr. Siemionow's project. "Technologies are constantly evolving as we try to extend or save people's lives. This creates new situations where we must be sure patients and research subjects are protected."

At Cleveland Clinic, quite a few members have served on the board for several years, which gives the IRB a depth of experience that helps in decision making. Dr. Lichtin and one other member have served on the IRB for more than a decade. Every year, members are asked if they wish to continue on the IRB.

"The dedication of some of the members of the board is quite exemplary," says Dr. Lichtin.

The IRB is made up of doctors, nurses, pharmacists, ethicists, psychologists, social workers, representatives of Cleveland Clinic's legal department and ombudsman office, and community members, all of whom are appointed by Cleveland Clinic's Board of Governors. The diversity of the group isn't accidental; it encourages valuable input from different perspectives. As mandated by the Department of Health and Human Service's Office for Human Research Protections (OHRP), at least one community representative must participate to bring the perspective of the patient community to the group. Currently, Andrew Trew, a bioethics professor and lecturer in philosophy at John Carroll University, fills that slot.

"I'm unusual, in a sense, because I also have a knowledge of bioethics and the legal issues nationally and internationally. I'm not really the typical community member, who would usually be someone like a policeman or a retired person."

The panel meets one afternoon every week for three to four hours, so it's a considerable time commitment for busy professionals. Many of the members have alternates who can sit in when the primary board member is unavailable. Trew acknowledges the difficulty of getting community members to come forward to serve on the uncompensated board; the time commitment may be too much for busy working people.

"I see this as partly my volunteer service to the community," says Trew, "and it's also very interesting to me because I see the cutting-edge medical developments, which reinforce my teaching of bioethics.

"I think what we're looking for when we meet is to examine all the issues and then to get to consensus. We have disagreements, and those are recorded, but these serve to foster discussion. This is not a rubber-stamp board."

OHRP's definition of research is any "systematic investigation ... designed to contribute to generalizable knowledge."

"If you're doing research," says Dr. Lichtin, "you have to have approval from an IRB." Hospitals or other research facilities without their own IRB can make use of another institution's board.

All research protocols, meaning the step-by-step process of how the research is conducted, and the informed consent form are reviewed at least annually. For very high-risk trials or procedures, such as Dr. Siemionow's work, the IRB may require the protocol to be reviewed more frequently, such as every three months or after each research participant is enrolled.

"Our review is to protect the research participants. Their safety and welfare are paramount." Linda Lewicki, R.N., Ph.D.

As part of its quality assurance program, the IRB also conducts random inspections of research as it progresses, says Dr. Lewicki. "We make sure the protocol, as it was approved, is being followed, and we confirm that the consent form was voluntarily signed."

The IRB also has the authority to suspend or terminate research if there's been an increase in risk that affects the safety and welfare of the research participants. If a research project is terminated, the board must inform OHRP of its action. If there is a possibility that scientific misconduct occurred, the board would refer the matter to Cleveland Clinic's Chief of Staff and a set of legal procedures would kick in.

In the United States, the response to serious research misbehavior such as the atrocities during World War II and the Tuskegee Syphilis Study was the formation in 1974 of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. This was followed by the publication in 1979 of the commission's *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. The *Belmont Report* has been a leading source of guidance regarding the ethical standards governing research with human participants in the U.S. Out of the work of the commission and the *Belmont Report* came the introduction of institutional review boards and the federal regulations governing them.

Says Dr. Lichtin, "We try the best we can to have all members of the institution who are involved in research – whether it's research coordinators, the nurses, the doctors, the principal investigators – to be cognizant of the great obligations they have in the research enterprise."

The simplest research procedure can involve risk. For example, even something as commonplace as drawing blood for a study is reviewed by the IRB, and the patient consent form for a blood draw spells out that fainting, bruising, infection and blood clots are potential risks.

With more involved procedures, the issues only become more complex. Phase I trials, which are early investigational trials of drugs, are designed to find a maximally tolerated dose of drug, and not to necessarily treat the patient's disease. Placebo studies always raise the thorny issue of the prudence of removing participants from the existing standard of care to test an untried drug that may do them more ill than good. Since medicine's first dictum is "do no harm," there are those who consider such actions unjustified or unethical.

But Dr. Lichtin emphasizes that the research participants are always at the top of the IRB's concerns. "The heart and soul of the Phase I study is closely monitoring for subject safety," he says. "You start with a very low dose and watch for any change, no matter how small, before progression to the next higher dose."

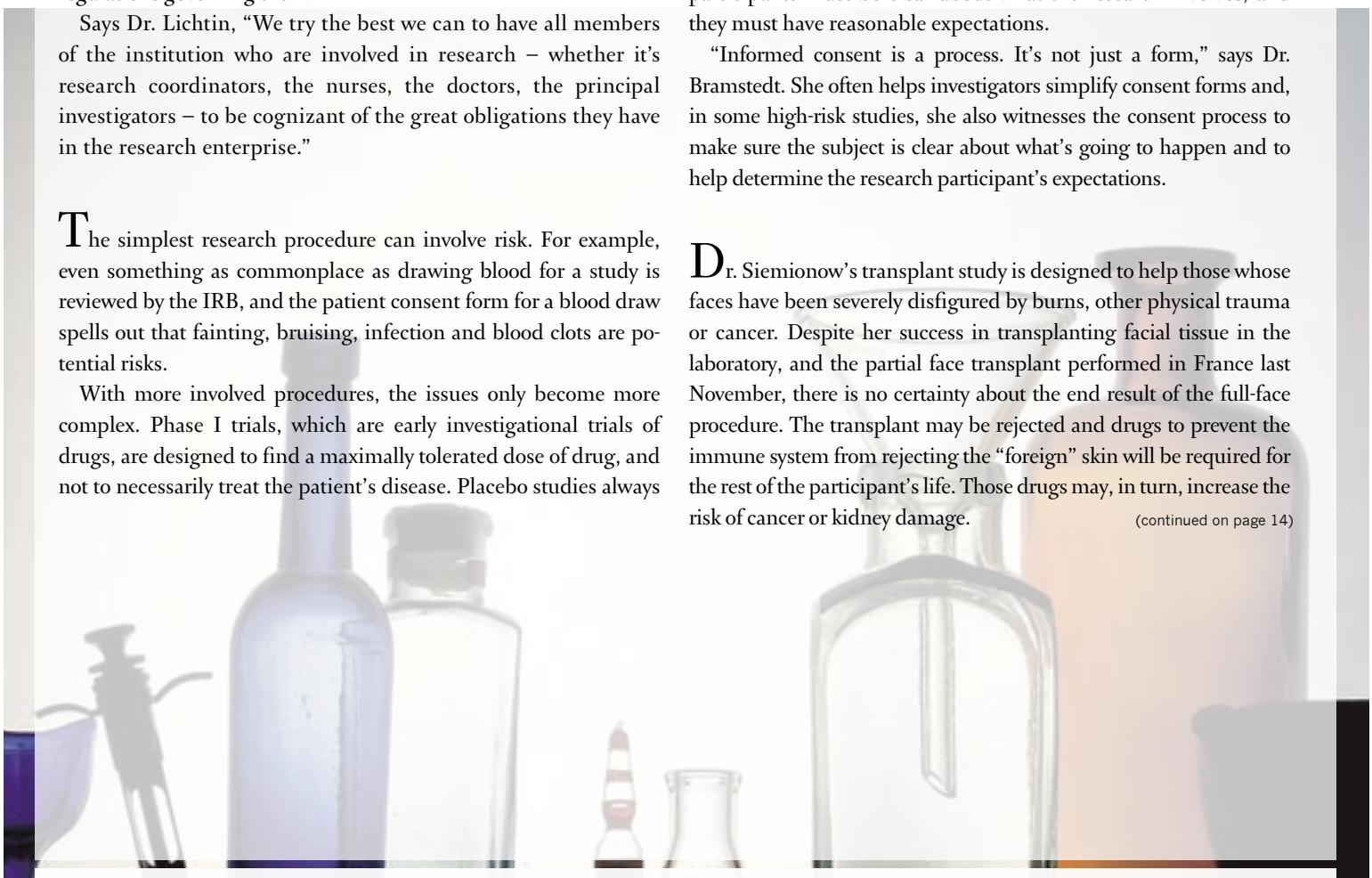
Placebo studies, he says, often are vexing for the IRB. If, for example, a participant on hypertensive drugs is placed in a placebo group and the research subject's blood pressure begins creeping up, the research coordinator would pull the person off the placebo before it reached dangerous levels. The participant also has another safety net: He or she may withdraw from the study at any time.

Informed consent is another area closely scrutinized by the IRB. The informed consent required by law involves far more than simply signing on the dotted line. Informed consent involves providing potential participants with sufficient information about the research in understandable language so they can make a voluntary and informed decision whether or not to participate. The potential participants must be clear about what the research involves, and they must have reasonable expectations.

"Informed consent is a process. It's not just a form," says Dr. Bramstedt. She often helps investigators simplify consent forms and, in some high-risk studies, she also witnesses the consent process to make sure the subject is clear about what's going to happen and to help determine the research participant's expectations.

Dr. Siemionow's transplant study is designed to help those whose faces have been severely disfigured by burns, other physical trauma or cancer. Despite her success in transplanting facial tissue in the laboratory, and the partial face transplant performed in France last November, there is no certainty about the end result of the full-face procedure. The transplant may be rejected and drugs to prevent the immune system from rejecting the "foreign" skin will be required for the rest of the participant's life. Those drugs may, in turn, increase the risk of cancer or kidney damage.

(continued on page 14)



"We try the best we can to have all members of the institution who are involved in research ... to be cognizant of the great obligations they have in the research enterprise." Alan Lichtin, M.D.

INSIDE THE IRB

Daniel Beyer, M.S., M.H.A., C.I.P., Executive Director, Cleveland Clinic Institutional Review Board

The Cleveland Clinic's Institutional Review Board (IRB) is charged with ensuring that people who volunteer for research studies are respected, informed and protected throughout the research process. The 13-member board, headed by Chairman Alan Lichtin, M.D., is made up of scientific members, such as doctors and nurses, and nonscientific members, such as a lawyer and a lay person from the community. The daily operation of the board is led by Executive Director Daniel Beyer, who oversees the administrative aspects for the review and monitoring of more than 2,300 active studies as well as the 100-plus study applications submitted each month.

CCM: How does one "train" to become an IRB member?

DB: Each appointed member completes an initial orientation session in ethics and human protection regulations and is mentored by an experienced IRB member. During weekly board meetings and annual retreats, members are given continuing educational updates. Members also are encouraged to participate in seminars and other conferences sponsored by national research associations, the Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services Office for Human Research Protections.

CCM: Take us inside a typical meeting.

DB: Members are given study protocols a week in advance so they can discuss the merits of the research before the full board convenes. The IRB chairman begins the meeting with general educational materials and current research-related news events. Each reviewer then offers his or her thoughts on the research study and the informed consent document. The IRB chairman encourages questions and comments from the various members, especially from non-scientific members and community representatives. After this discussion, a motion is made to approve, conditionally approve pending minor changes, or table the study protocol for substantial revisions. The research may not begin until the IRB has granted full approval. An expedited review process may be held for research involving minimal risks, such as routine collection of blood or the use of existing records or data.

CCM: After a study is approved, is the IRB's job over?

DB: After the study protocol and consent process are approved, the investigator is charged with conducting the research exactly as it was approved by the IRB. Any changes to the protocol or consent must be re-reviewed and approved before they can be implemented. The IRB also reviews study progress reports at least annually, or sooner if it determines the level of risk requires more frequent monitoring. In 2001, a quality improvement program was initiated to monitor and inspect approved studies in an ongoing manner. The purpose of this program is twofold: one, to assess compliance with federal regulations and IRB policies; and two, to educate the research team about their ethical and regulatory responsibilities when conducting research.

CCM: Do IRB members get paid for their service?

DB: The FDA guidelines do not specifically preclude compensation for IRB members. However, Cleveland Clinic IRB members are not paid for their services.

CCM: Is there a governing body for IRBs?

DB: The National Research Act of 1974 established the modern IRB system, including the membership, composition and criteria that an IRB must follow with respect to research involving human subjects. Cleveland Clinic signed an agreement with the U.S. Department of Health and Human Services Office for Human Research Protections assuring that it will comply with the regulations for protecting human subjects in research.

"Because this is a first time for use with humans, the procedure raised ethical concerns," Dr. Lichtin notes. "The immunosuppression, with all its lifelong risks, was a big area of discussion for us."

The board had to deliberate a number of issues: the importance of the face to one's identity; how this procedure was different from cosmetic surgery; whether or not the risks involved in placing a patient on a lifelong regimen of immunosuppressants to prevent rejection are worth the benefit; and the idea that such a radical procedure, which includes the risk of death, would be attempted for a condition that is not, on the surface, life-threatening.

"Some people might say that a person becomes so depressed from losing their way of being viewed by the world that it is life-threatening," observes Dr. Lichtin. During the IRB review, he brought in psychiatrists to discuss their relationships with patients who have severely disfigured faces and to help the board explore the issues of lifesaving versus life-enhancing treatment.

The IRB's deliberations were not made any easier when both Britain's Royal College of Surgeons and France's National Ethics Advisory Committee released position papers against attempting a human facial transplant. The British and French expressed many worries, from a participant being left without a face if the operation failed, to the hypothetical use of such a procedure for cosmetic or criminal purposes. They wondered if society is ready for such an undertaking. Since the face is the seat of identity, should one person receive the face of another person?

Dr. Lichtin called in Cleveland Clinic's own bioethics staff to help sort through the objections, and the board learned that although the procedure was not necessarily lifesaving, it had the potential to restore quality of life. They learned the recipient would not look like the donor because the transplant essentially involves skin and not the muscle and bone that truly gives each face its unique appearance.

"This is a wonderful example of not only can-do technology, but also of asking the second question: Ought we to do it?" says Trew, the bioethicist from John Carroll University. Photographs that Dr. Siemionow brought in of potential candidates for the operation helped to form his response. Trew looked at the photos and was taken by the willingness of those people to be considered for such a groundbreaking procedure.

"They really are going to be pioneers to help other people. They stand to gain, but they also stand to lose – perhaps even lose their lives," he says.

Trew is convinced that Dr. Siemionow's work represents a major breakthrough in transplantation and should go ahead. "After that, yes, if it works, then I think the public comes on board," he says, just as it eventually did after the world's first heart transplant decades ago.

Over the months of debate, those board members who expressed concerns against the full face transplant protocol had their questions and concerns addressed. In the end, after considering the arguments, criticisms and support, including Dr. Siemionow's 20 years of research and the appreciation that the transplant would not involve an actual "face," as Hollywood or the media might depict, but skin, fat, nerves and blood vessels, the board voted unanimously to approve the procedure.

"I'm impressed by the fact that the IRB did take 10 months, that we didn't just say, 'Oh, this is first to market,'" says Trew. "There's no question that Dr. Siemionow is an amazingly sincere and dedicated surgeon. That's very reassuring to me."

Dr. Siemionow says that she learned a lot from the lengthy IRB process and agrees that faster approval would have suggested that there hadn't been enough of a discussion.

"We are hoping to do it right," she says. "Not only in a technical and scientific way, but also in a humanitarian way." For the IRB, that's exactly the type of patient protection it wants to ensure.

"This is a wonderful example of not only can-do technology, but also of asking the second question: Ought we to do it?" Andrew Trew

Frontiers can be frightening places. Unruly dilemmas stalk the wild edges of science and medicine. In 1803, explorers Lewis and Clark could count on Sacagawea, their Shoshone guide. But who counsels the physicians, scientists and families afoot on the frontiers of medicine?

Ethics at the Edge

"We recognize that medicine puts families and researchers in many vexing positions," says Eric Kodish, M.D., Chairman of Cleveland Clinic's Department of Bioethics. "Bioethics can help people involved in this type of situation to think through their decisions."

The field of modern bioethics developed in the 1960s, and in its early years, reflected the spirit of the times. But soon new medical technologies were complicating end-of-life decision making. Philosophers, religious scholars and consumer advocates began asking questions about who had the authority to make these decisions, on what basis and in whose name. "Physicians began to play a larger role in the field of bioethics a decade or so later," says Dr. Kodish.

Today, bioethics is a valued part of the medical establishment and, while there is no board certification for bioethics, most hospitals have ethics committees; ones that don't rely instead on the ethics committee at the nearest hospital. Many bioethicists are practicing physicians like Dr. Kodish; others represent disciplines ranging from law to theology.

While relatively new, bioethics has been thrust into the public eye over the past few years, propelled by such hot-button topics as stem cell research, human cloning, "morning-after" contraceptives, withdrawal of the painkiller Vioxx from the market and the emotional right-to-die battle over the late Terri Schiavo, the Florida woman who spent years in a persistent vegetative state.

The five members of Cleveland Clinic's Department of Bioethics are kept busy not only with patient-centered medical conundrums, but also with rapid developments in clinical research.

"We have the busiest ethics consultation service in the United States," says Dr. Kodish. "We do more than 200 ethics consults every year and are available on call day and night, seven days a week. Most calls come from physicians and nurses, but we also hear from families, chaplains and others."

Dr. Kodish sees his job as "asking the right questions. We begin from a position of humility. We have to be good listeners. Our job is not to impose our own goals. It is to facilitate a collaborative discussion that leads everyone to do the right thing. The patient is the ultimate authority on his or her own care."

Established in 1983, Cleveland Clinic's Bioethics Department is part of its Division of Clinical Research, which reflects the increasingly complex ethical world of research involving stem cells and genomic and tissue transplantation. A member of Dr. Kodish's department sits on the Institutional Review Board and another serves in a position called "research subject advocate," to assure that the safety of the study volunteers remains the highest priority.

Bioethics staffers review consent forms and processes, and serve as advisors to the Cleveland Clinic's Institutional Review Board. They also provide ethics consultations and education to patients, research participants and family members as well as to other Cleveland Clinic professionals. And they help in assessing the suitability of transplant candidates for donor organs.

"The goal of clinical research is to learn and advance medical knowledge," says Dr. Kodish, "but human subjects must not be exposed to risks that have no potential benefit."

Bioethics is a young discipline, and there is as yet no formal path for career aspirants. Dr. Kodish got involved through his specialty of pediatric oncology. Others come to bioethics through law, social science, nursing or religious studies. There is, however, a shortage of trained bioethicists nationwide. To meet this need, Cleveland Clinic, in collaboration with University Hospitals of Cleveland, Case Western Reserve University and MetroHealth Medical Center, is developing the Cleveland Fellowship in Advanced Bioethics. Based at Cleveland Clinic, the program will provide practical, experiential learning and academic rigor for scholars launching a career in bioethics, says Dr. Kodish. The first class will enroll in 2007. "We have all the clinical, research and institutional resources – plus the resolve – to make Cleveland the bioethics center of the world."

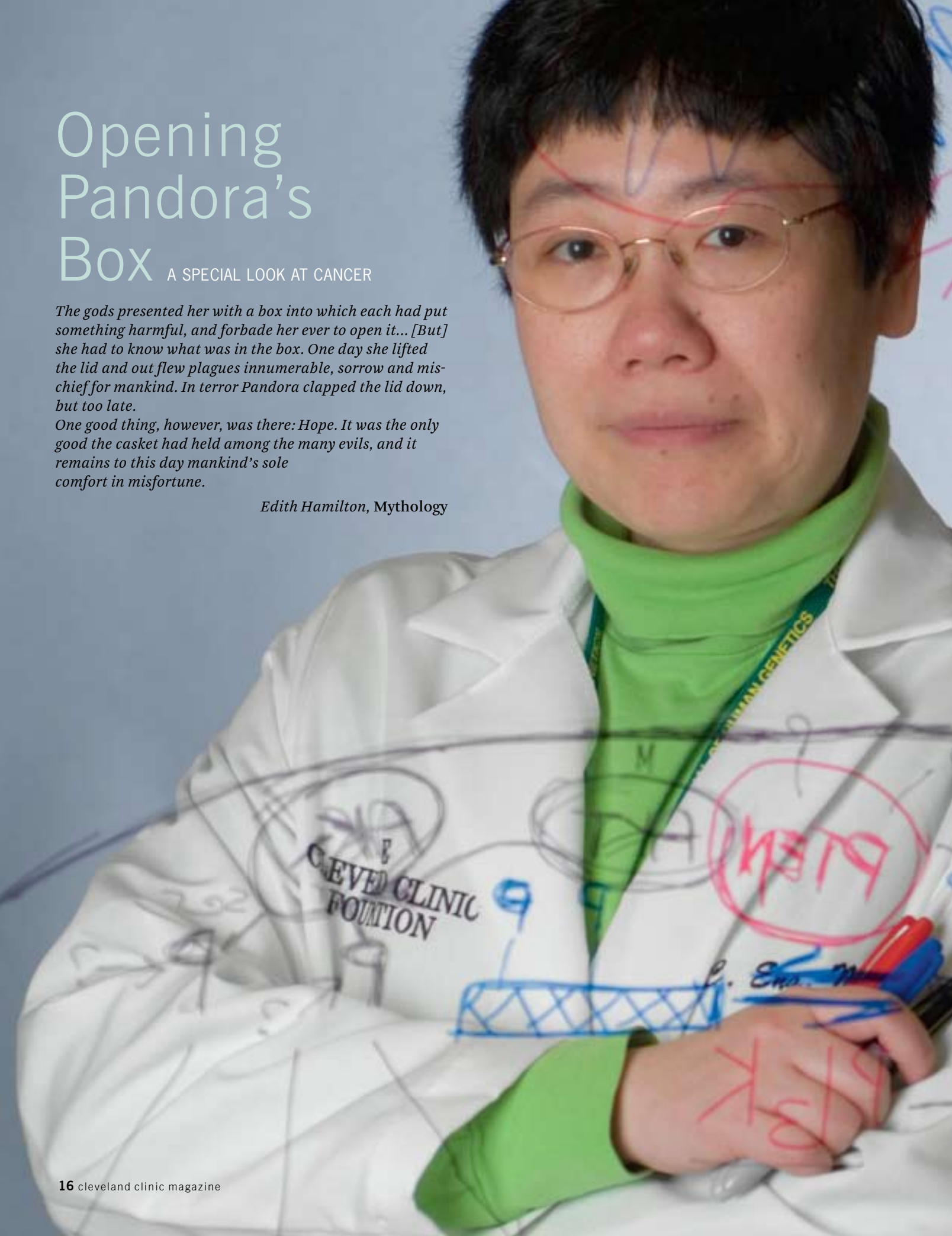
Opening Pandora's Box

A SPECIAL LOOK AT CANCER

The gods presented her with a box into which each had put something harmful, and forbade her ever to open it... [But] she had to know what was in the box. One day she lifted the lid and out flew plagues innumerable, sorrow and mischief for mankind. In terror Pandora clapped the lid down, but too late.

One good thing, however, was there: Hope. It was the only good the casket had held among the many evils, and it remains to this day mankind's sole comfort in misfortune.

Edith Hamilton, Mythology



One disease. That was how we once viewed cancer. Now, we know better.

Cancer is not a single disease – it is many. More than 200 at last count. And therein lay the problem: Each cancer has a different cause, and each will have its own unique cure.There is no "magic bullet" for cancer. No vaccine. No pill. No treatment that can zero in on an individual's particular cancer and eradicate it with a single, targeted therapy.

No cure for cancer. Yet.

Here is what we do know: Cancer starts deep in the cell, within the DNA. A tiny change happens, causing the cell's inner workings to malfunction. The cell begins to multiply uncontrollably. Major body systems are ravaged. Lungs. Bones. Brain. Liver.

Broken genes. Lives, changed forever.

Charis Eng, M.D., Ph.D., Chair of the Genomic Medicine Institute, has already connected one broken gene, PTEN, with breast cancer. Her work may throw light on what makes a gene go awry. It may produce new targets for therapy, new ways to diagnose and prevent cancer.

The box is open. But the work ahead is difficult.

"There's a lot to learn," says Dr. Eng. "What mutations make you vulnerable to one cancer or another? Where do they happen? We're searching for clues – clues that will one day lead us to cures."

"I did it to save my life."

Why does Cleveland Clinic study genes? Patients like Kelly, for one. In 1994, gene researchers doing work similar to that of Cleveland Clinic discovered a genetic alteration in a gene called BRCA1. It was a mutation that came attached to a disease: breast cancer.

BRCA1 gene mutations can run in families. Breast cancer shows up at a younger age in these families and it often occurs in both breasts. It can affect the men, as well as the women, in the family.

Twenty-five-year-old Kelly has the BRCA1 gene mutation. It means she has up to an 80 percent chance of developing cancer. She has a family history of breast cancer: mother, grandmother, great-aunt. All were diagnosed before they turned 40.

"BRCA1 changes everything. Your life, your timetable isn't yours anymore. Want to travel? Buy a house? Gotta do it now. Have kids? Don't wait," says Kelly.

"I knew the odds weren't in my favor. Having the gene test done, getting the results was difficult. But early diagnosis is so critical."

Wanting to see the world, Kelly jetted to New Zealand last spring. In November, she was forced to return: Something had shown up on her ultrasound. A biopsy confirmed the cancer. Kelly had to make a difficult decision.

She decided to have a mastectomy. Joseph Crowe, M.D., performed the operation. "It was small, but we got it early," says Dr. Crowe.

But there was more. Because she has a BRCA1 mutation, Kelly elected also to have her healthy breast removed. She wanted to reduce the risk of the cancer returning.

"I did it to save my life," she says. "If there was another way – if I could take a pill, get a shot – would I have done that? Absolutely."

Groups of researchers meet. Plans are laid. Problems are attacked. Solutions are found. Analyses ensue.

"We need to read every word."

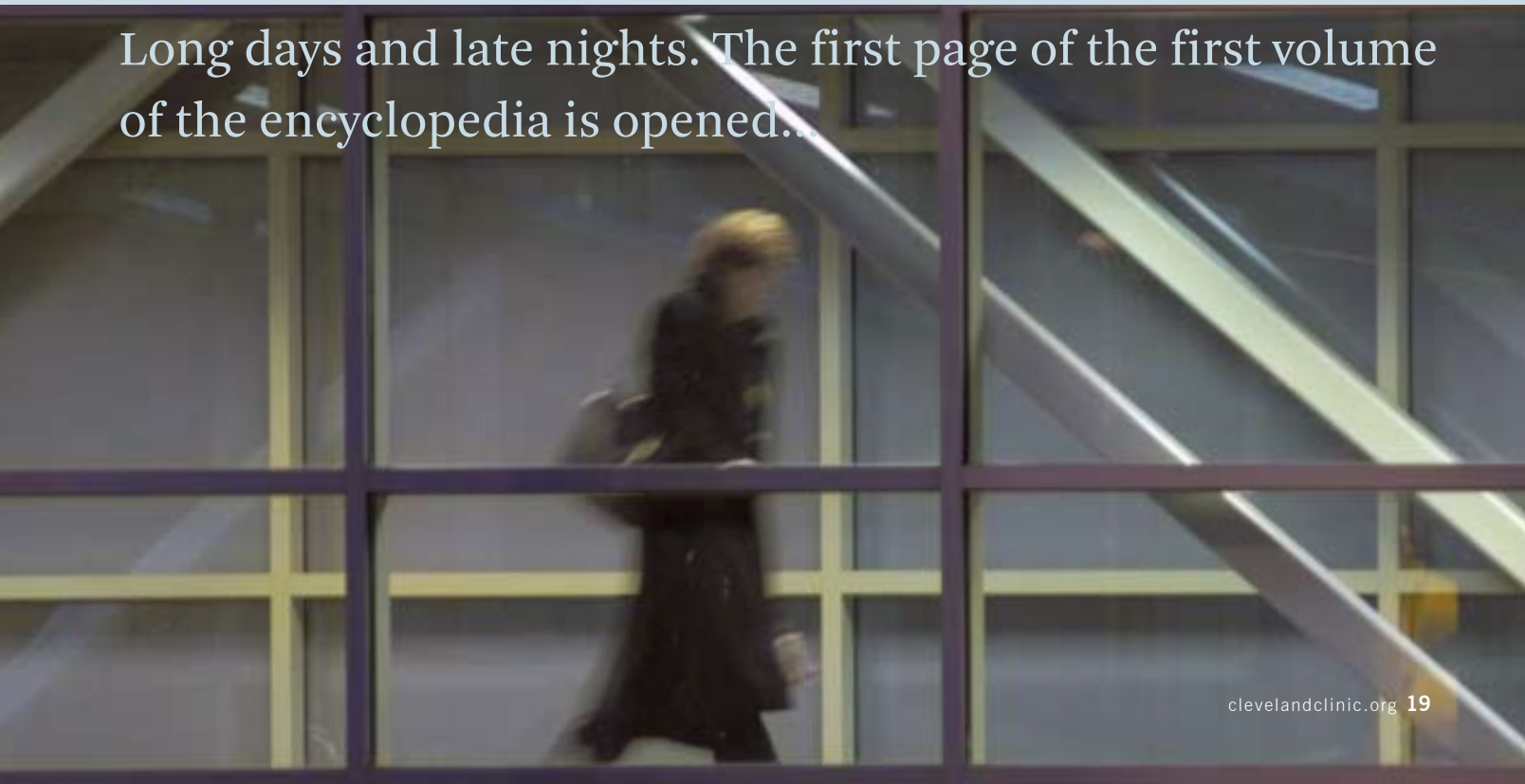
Every gene is like a vast encyclopedia, containing huge amounts of information. Put the volumes with all their sentences, words and letters in the right order, and everything works, it all makes sense. Move a sentence, misspell a word or drop a letter and the information is wrong. In a person, that error can mean cancer.

"As researchers, we need to read every word and sentence in every volume of this encyclopedia to find if there are errors and where they are," says Dr. Eng.

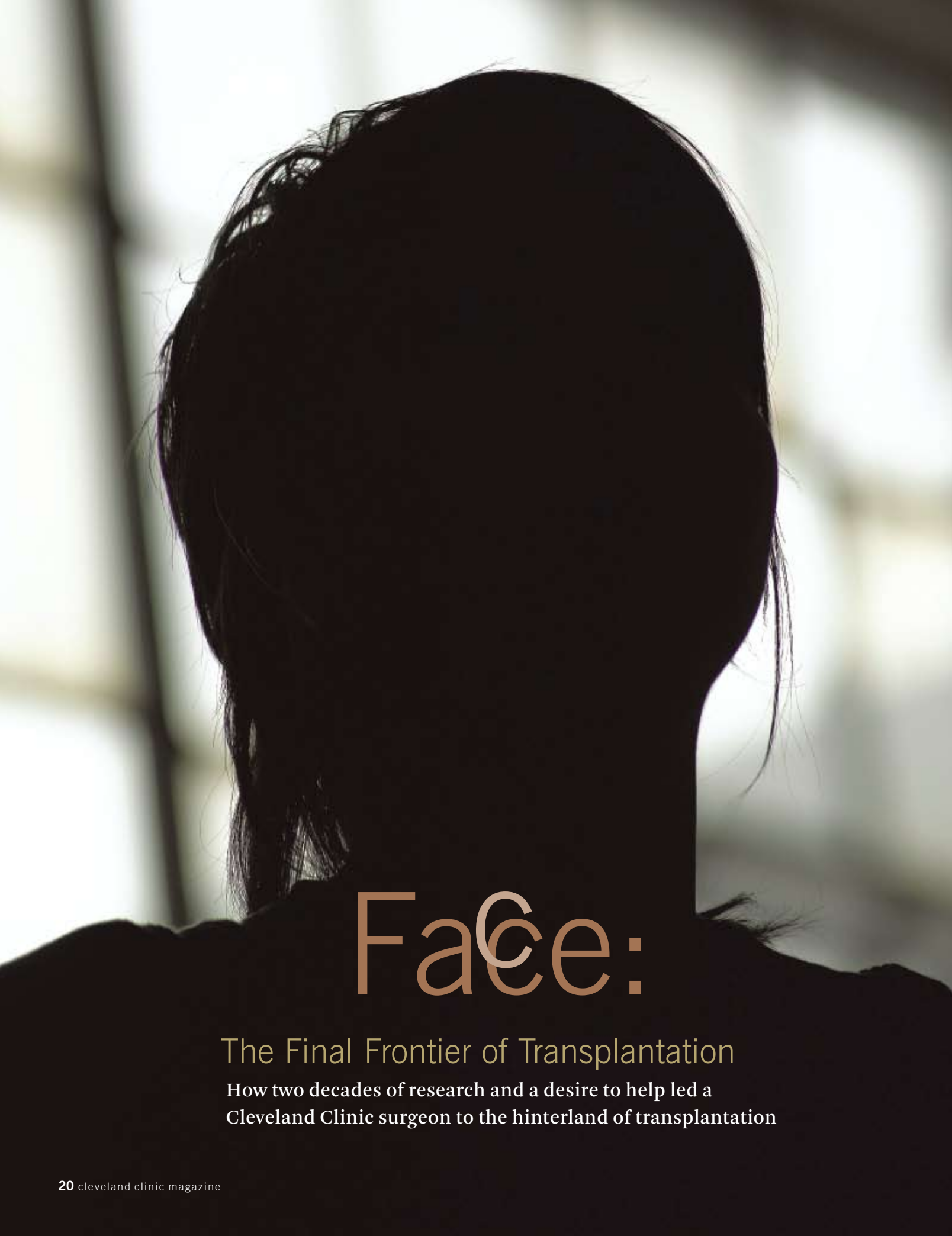
To study genes, Cleveland Clinic researchers need genes to study. So they created a biorepository. Genetic samples are sent to Cleveland Clinic from around the world. Donors want to know: "Will I get cancer? Why me? Can it be cured?"

Samples are logged in and processed. Some of the cells are grown in a way that allows them to perpetuate. Weeks pass as they grow and divide. In the end, different materials are separated out, each going into separate freezers. DNA, RNA, protein, live cell lines – all are held in stasis waiting to be called to action.

Groups of researchers meet. Plans are laid. Problems are attacked. Solutions are found. Analyses ensue. DNA sequencing. Protein function studies. Microarrays. Long days and late nights. The first page of the first volume of the encyclopedia is opened ... ✪



Long days and late nights. The first page of the first volume of the encyclopedia is opened...



Face:

The Final Frontier of Transplantation

How two decades of research and a desire to help led a Cleveland Clinic surgeon to the hinterland of transplantation

Some call it science fiction. Others compare it to a Hollywood fantasy. But for Maria Siemionow, M.D., Ph.D., D.Sc., this is strictly reality — a full face transplant — and she may be the first physician in the world to perform it.

Dr. Siemionow, who heads Cleveland Clinic's Section on Plastic Surgery Research and is on staff with Cleveland Clinic's Transplantation Center and departments of Orthopaedic Surgery and Immunology, has been in the spotlight since Cleveland Clinic's Institutional Review Board unanimously approved her proposal for performing a full face transplant in October 2004. (See article, page 10.) The media barrage hit with full force after last fall's partial face transplant in France.

"Let's see, I've talked to Katie Couric, The Today Show, Anderson Cooper, CNN, Nightline, CBS, NBC," she says, rattling off the names. "Initially we decided we weren't going to give any media appearances, but at some point it became so important we felt it was necessary instead of a continued 'no comment' from Cleveland Clinic."

The entire concept prompts people to ask Dr. Siemionow whether she's seen the 1997 movie "Face/Off," starring John Travolta and Nicholas Cage. She has watched it, and her immediate response is that it is just a movie — pure fiction that portrayed an undercover agent who took not only the face, but also the voice and body of a major criminal. By contrast, Dr. Siemionow's work is not about identity transplantation. What she plans to do is transplant facial skin, blood vessels and nerves from one human to another.

Dr. Siemionow has spent the last 20 years involved in intensive transplant research. She has published scores of articles on composite tissues allograft transplantation, which are transplants of organs composed of multiple tissue types, such as what would be used for a face transplant. While she says the technique for performing a full face transplant isn't necessarily new, the public's fascination with the newness of the concept isn't going away.

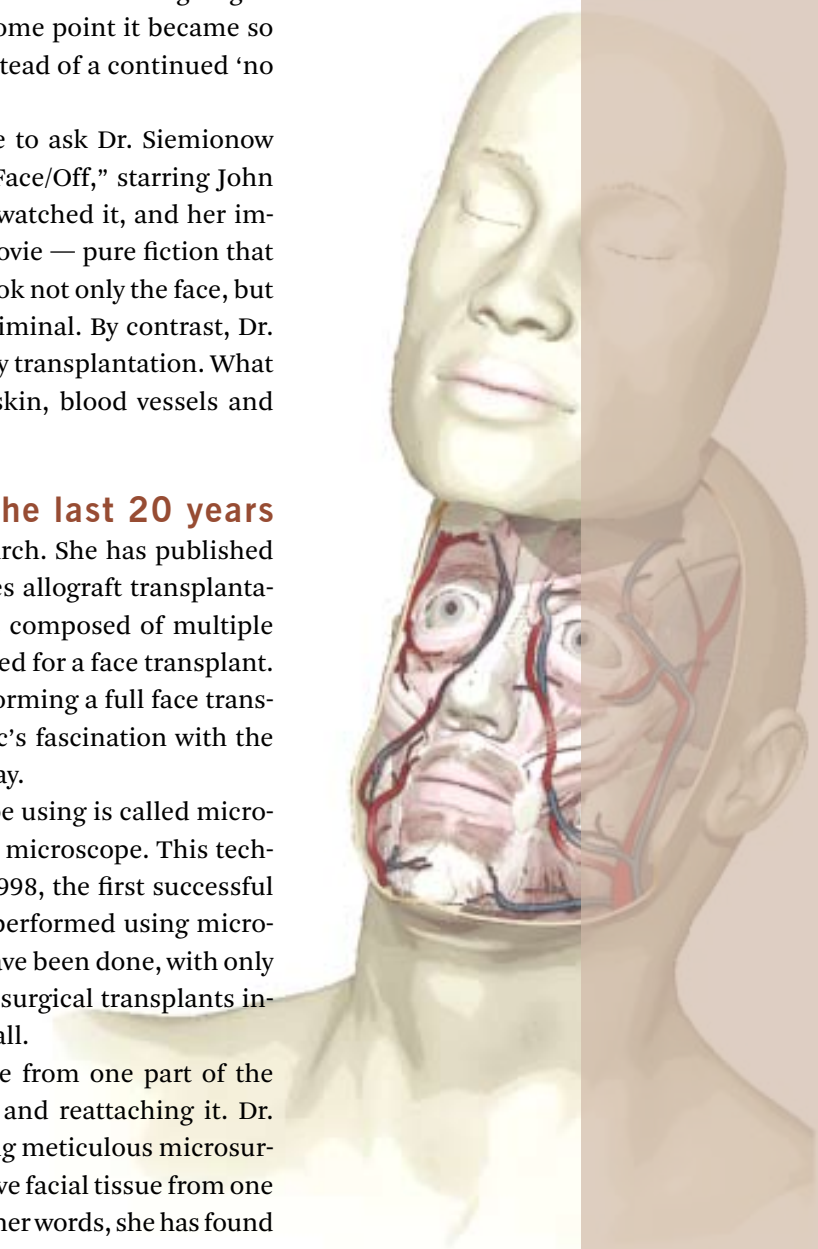
The technique Dr. Siemionow will be using is called microsurgery — surgery performed under a microscope. This technique has been used since 1980. In 1998, the first successful hand transplant from a cadaver was performed using microsurgery. Today, 25 hand transplants have been done, with only two failures. Other examples of microsurgical transplants include a larynx, knee and abdominal wall.

Microsurgery involves freeing tissue from one part of the body, transferring it to another part and reattaching it. Dr. Siemionow has shown that, by applying meticulous microsurgical techniques, it is possible to remove facial tissue from one cadaver and transfer it to another. In other words, she has found a new application for a proven technique, and although the surgery might sound bizarre to some, she explains that it really is just about reconstructing a face.

How it Works

A facial transplant will require harvesting facial skin, blood vessels and nerves from the donor. The harvested tissue then will be transplanted onto the recipient by a team of plastic surgeons, transplant surgeons, anesthesiologists and others. Because the recipient's bones and underlying muscle, cartilage and fat will be left in place, the recipient's "new" face will bear little resemblance to the donor's face.

Illustration courtesy of The Plain Dealer.



"The face is the most visible part of you."

Maria Siemionow, M.D., Ph.D.

"This is not someone walking around with your loved one's face on the street," Dr. Siemionow emphasizes. "This is about helping someone badly disfigured regain their quality of life."

Gratification for the scientific advances and microsurgical techniques Dr. Siemionow has mastered comes in the form of now helping those desperately in need. She explains, "What it is not about is vanity. This is not about someone getting a beautiful face, or thinking you'll do it for better appearances or looks. These are people who are not getting out of their houses – they're hiding."

Those of us who haven't coped with a severe or disfiguring facial deformity cannot begin to understand the deeply personal and emotional pain involved, she says. Some go out shopping only at night to avoid people. Others stay indoors. Some have been abandoned by family or spouses. Still others endure constant awkward stares and crude comments from unthinking people.

"The face is the most visible part of you," Dr. Siemionow says quietly. "Some of these people cannot open their mouths or close their eyes." Among them are those burned or scarred in terrible accidents such as house fires, car crashes and explosions. "Their faces have been transfigured into something unrecognizable."

For people who suffer from severe facial trauma, particularly burns, limited help is available. Skin grafts taken from other areas of the body – buttocks, thighs or abdomen – often leave patients with an end result that resembles a sloppy patchwork quilt. The transplanted skin is often thick, discolored and offers little pliability.

Dr. Siemionow says that transplanted facial skin is the only real substitute for damaged facial skin – it allows for the same pliability, thickness and stretchability. "Nowhere else on a person's entire body does an equally good substitute exist."

A face, excluding a scalp, would require nearly 700 square centimeters of skin. "That's a foot by a foot," Dr. Siemionow says, measuring with her hands. "That's a lot of skin." She adds that if a scalp were needed, nearly 1,200 square centimeters of skin would have to be harvested.

It will take about four and a half hours to harvest the facial skin from the donor, and at least 15 hours for a team of plastic surgeons, transplant surgeons, anesthesiologists and many others to perform the actual transplant.

In preparation for the donor tissue to be transplanted, the damaged skin of the recipient is removed along with scar tissue. Bones and underlying muscles are left in place. The harvested facial graft is then transferred from the donor to the recipient, and the arteries, veins and nerves are "hooked up" using microsurgical techniques. To ensure that the transplant initially "takes," good perfusion, or blood flow, is necessary in the first few minutes after the operation is complete.

"The surgical technique is ready," says Dr. Siemionow. "Now all we need is the right transplant recipient."

She says the "right" recipient is someone who is psychologically stable and who has weighed the risks and benefits of a full face transplant. This person must be strong enough and stable enough to undergo the rigorous transplant and ensuing changed life thereafter.

Potential recipients would be screened to determine if they are psychologically fit to withstand the transplant. Through the process of informed consent, they also would be made fully aware of the potential risks of the procedure. One of these risks is transplant rejection. If that were to happen, the newly transplanted facial skin would die. "If the transplant fails, we are prepared to transplant skin from other body areas onto the face," Dr. Siemionow says. Other risks to be weighed include the side effects of lifelong immunosuppressive therapy, which include skin cancer, anemia, impaired wound healing and possible kidney failure.

In addition to finding the right recipient, the team has to find the right donor. Criteria include matching the gender, skin color and age to the recipient. The procurement procedures for harvesting the face would be the same as any other organ transplant: The donor's family would be fully informed about the procedure before consenting.

Several months have passed since French surgeons performed the world's first partial face transplant. Interest has been renewed since the patient has been giving media interviews, her face showing slight scarring and her lips yet unable to easily move. Her doctors predict she will resume full use of her facial muscles.

As for the eventual success rate of a full facial transplant, Dr. Siemionow says this is unknown since all of her studies were conducted on experimental and cadaver models. However, she remains optimistic. "We really only have solid information based on hand transplants that show a favorable outcome, the longest one being done more than seven years ago."

She also is among those researchers worldwide who are looking for ways to reduce the massive amounts of immunosuppressive drugs transplant patients must take to prevent rejection. In preliminary laboratory studies, she has found that it is possible, after short course, to successfully stop immunosuppressive therapy after transplantation with minimal side effects.

Dr. Siemionow hopes to bring her immunosuppressive therapy research to human trials in solid organ transplants – kidney and liver, for example – in the very near future. Without the need for lifelong immunosuppressive therapy, face transplantation could become part of the full armamentarium of plastic and reconstructive surgery options for people who are badly disfigured. ◘

To read more about Dr. Siemionow and her work, go to clevelandclinic.org/clevelandclinicmagazine.

"The surgical technique is ready," says Dr. Siemionow. "Now all we need is the right transplant recipient."

Never Too Young

Strokes can happen at any age...

even before birth

The signs were so subtle they could easily have been overlooked by any mother, especially a first-time mom. But they did not escape Shannon Von Gunten: her 3 1/2-month-old son, Aidan, was reaching for things using only his right hand. Was this just an aberration, or was there something wrong with her newborn child?

For 18-year-old Yevgenia Baron, a severe headache accompanied by bouts of dizziness prompted her to make a trip to the emergency room. She didn't receive a specific diagnosis but was given a prescription for ibuprofen and discharged. Two days later, after her symptoms worsened, she returned to the ER, where an MRI was done.

Though ages apart, Aidan and Baron shared a common and frightening diagnosis: both had suffered a stroke. In a society where awareness of stroke generally tends to be associated with adults, "pediatric stroke" can seem like a contradiction in terms. Not so, says Cleveland Clinic pediatric neurologist Neil Friedman, M.B., Ch.B. "Children suffer strokes just like adults do. The problem is that these strokes tend to be under-recognized and under-diagnosed."

Numerous recent studies estimate that the incidence of pediatric strokes – those occurring before birth to age 18 – exceeds six per 100,000 children every year. Dr. Friedman, who specializes in pediatric stroke, says that even at this conservative estimate, the incidence of pediatric stroke is almost twice that of pediatric brain tumors. "People know about pediatric brain tumors. We need to begin educating them on stroke."

In a society where awareness of stroke generally tends to be associated with adults, "pediatric stroke" can seem like a contradiction in terms.

Pediatric stroke can strike the unborn or those just barely into their first few days of life. Perinatal stroke occurs from 28 weeks into pregnancy to the first seven days of life, while neonatal stroke occurs in the first 28 days of life. Among perinatal and neonatal strokes combined, 10 percent are caused by cardiac disease in the child, 30 percent to 50 percent are caused by coagulation disorders in either the child or mother, and in more than 30 percent of cases the cause is unknown. Stroke affects newborns more than any other pediatric age range. The incidence of newborn stroke is more than one in 2,500 live births, which translates into about 1,000 to 1,500 newborn strokes per year.

Aidan Von Gunten had such a stroke. Although newborn strokes typically are the most challenging to recognize, Aidan's mother credits the early childhood development class she took in college and her subsequent job as an early intervention specialist working with developmentally disabled children for providing her with the awareness to observe when Aidan's physical development was peculiar at 3 1/2 months.

Aidan Von Gunten

"When I noticed he had started reaching for objects with only his right hand and would only kick his right leg, it was a big red flag to me," says Von Gunten. "His left leg and arm would just lay there, as if he didn't realize his left side existed. He was learning to open his hand, and when I stroked the back of his right hand, it would open readily, but his left hand wouldn't."

Von Gunten says that she set herself a four-week time limit "to observe and work with Aidan," but when the discrepancy became progressively worse, she made an appointment with Aidan's pediatrician, who referred her to Dr. Friedman. Results of an MRI taken when Aidan was 5 months old showed a stroke had occurred on the right side of his brain.

"The difficulty in observing physical or cognitive problems in infants who are still developing and not yet able to communicate, coupled with the lack of recognition that stroke can occur, is the main reason pediatric stroke is under-recognized and under-diagnosed," says Dr. Friedman. "Fortunately, Shannon was able to pick up on the subtle symptoms of Aidan's stroke quite early."

Stroke symptoms can be overlooked even by parents of older children who are more developed and able to communicate problems they are having. Dr. Friedman recalls one instance where the initial evidence of stroke occurred when a 5-year-old child dropped a toothbrush, then was unable to use her arm. The parents, whom Dr. Friedman describes as "intelligent, educated individuals," dismissed the odd event and put the child to bed as usual that Saturday night. By the next day, the child began slightly dragging one leg. After being sent to school that Monday, the school contacted the parents later in the day to alert them that something was seriously wrong with their child.

"It turned out the child had a stroke secondary to chicken pox," says Dr. Friedman.

According to the Children's Hemiplegia and Stroke Association, the prevalence of stroke among children who have chicken pox is estimated to be between one in 6,500 to 15,000 children. "Though rare, several studies have shown a relationship between chicken pox and childhood stroke," says Dr. Friedman. "In such cases, the chicken pox infection generally precedes the stroke by weeks to up to six months." Dr. Friedman says that having children vaccinated against chicken pox may prevent these related strokes from occurring, though "we do not yet know if the chicken pox vaccination has, or will, impact the incidence of varicella [chicken pox] stroke – though most people in the field think it has."

The good news is that children who survive strokes generally have better outcomes than adult stroke survivors.

Stroke also can occur in healthy children who experience a significant blow to the head, such as when they are playing sports or suffer whiplash from an automobile accident. Sometimes the first symptom of stroke from head trauma can be a severe headache that might not even occur on the same day of the injury.

While that was not the case with Yevgenia Baron's headache – congenital heart disease was the underlying cause of her stroke – she offers cautionary words of advice to others, based upon her own ER experience:

"Beyond knowing yourself, make the doctors understand that you understand your body well enough to know when something's not right. And if you don't receive a diagnosis, don't accept that at face value. Ask the doctors if they've done everything they can," says Baron, who is now 21.

Despite her delayed diagnosis, Baron says, "Considering what could have happened, I still feel lucky. Today I lead the normal, active life of a college student, with only occasional difficulty using language when I feel nervous or overly tired."

Early historical evidence of pediatric stroke was mostly anecdotal. Now, thanks to greater awareness and improved cranial imaging technology, it is becoming increasingly recognized and diagnosed by physicians. "MRI is the best way to diagnose a pediatric stroke," Dr. Friedman says. "It gives a very detailed analysis."

Treatment, however, is more problematic. Because most pediatric strokes are discovered only after the fact, the opportunity to treat them is generally long past. "In an ideal world, we would see the child soon after a stroke occurs, quickly confirm their diagnosis and treat them accordingly," says Dr. Friedman. "Instead, what physicians most often end up treating is the underlying cause of the stroke, such as a heart defect or clotting disorder, which mainly helps prevent a stroke from recurring."

Clot-busters, a treatment used on adults, have only been used on children on rare occasions. "A recent study showed that the average time from onset of stroke symptoms to seeing a doctor was 28 hours, with confirmed diagnosis typically only made at about 34 or 35 hours," says Dr. Friedman. "This is far beyond the three-hour window for clot-busting drugs to be effective." These drugs, as well, have not been properly tested for safety or approved for use in children.

The good news is that children who survive strokes generally have better outcomes than adult stroke survivors. Children's brains have much greater plasticity, meaning that the healthy parts of their brains often are able to adapt and take over functions that normally would have been directed by the area of the brain damaged by stroke. "In adults, we are also dealing with underlying degenerative vascular disease such as atherosclerosis, which can complicate treatment and recovery," says Dr. Friedman.

Nevertheless, Dr. Friedman cautions, a majority of children stroke survivors will have residual and persistent neurological and/or cognitive impairment.

When 5-month-old Aidan Von Gunten's stroke was diagnosed, Mrs. Von Gunten knew that the sooner he began receiving rehabilitation therapy, the greater his chances were of gaining better use of his left arm and leg and having a more normal life.

"Rehab is all about function," says Barbara Wechsler, M.D., Rehabilitation Program Director at Cleveland Clinic Children's Hospital Shaker Campus. "When we can't restore function, we teach the patient how to compensate. It's about maximizing quality of life and enabling children to fully participate in society."

Pediatric stroke patients will frequently lose function of the muscles on one side of their body. Over time, those weak muscles change from initially being flaccid to demonstrating spasticity, which interferes with the child's ability to move. Physical therapists teach the children how to walk, run, climb stairs and move from one surface to another.

"Aquatic therapy helps tremendously. It is safe – the child cannot fall – and it is the most efficient way to rebuild muscle strength. The buoyancy of the water helps the children succeed," Dr. Wechsler explains.

Occupational therapists help the children regain independence with activities of daily living, including eating, dressing and toileting. They also work on fine- and visual-motor activities. “And playing, too,” says Dr. Wechsler, “because that’s the children’s occupation – they go to school and they play.”

Strokes can cause various speech problems, from slurred speech related to muscle dysfunction to aphasia, which is the inability to articulate thoughts, read or write. This sudden loss of the ability to communicate is both scary and frustrating to the child and family and is addressed by speech and language therapists.

“If a child loses his or her ability to use language because of aphasia, there are all sorts of strategies to help the child retrieve their language skills and communicate,” says Dr. Wechsler.

The speech and language therapists also work on the cognitive portion of the child’s rehabilitation program.

“For any child with a brain injury of any kind, a cognitive deficit sometimes remains after the child has improved physically,” Dr. Wechsler explains. “The child realizes this and will tell us he feels ‘stupid.’ When the child feels bad about him - or herself like that, it can lead to behavioral problems. Access to appropriate psychological and educational interventions at all stages of recovery is crucial to enabling these children to maximize their potential.”

Neil Friedman, M.B., Ch.B.

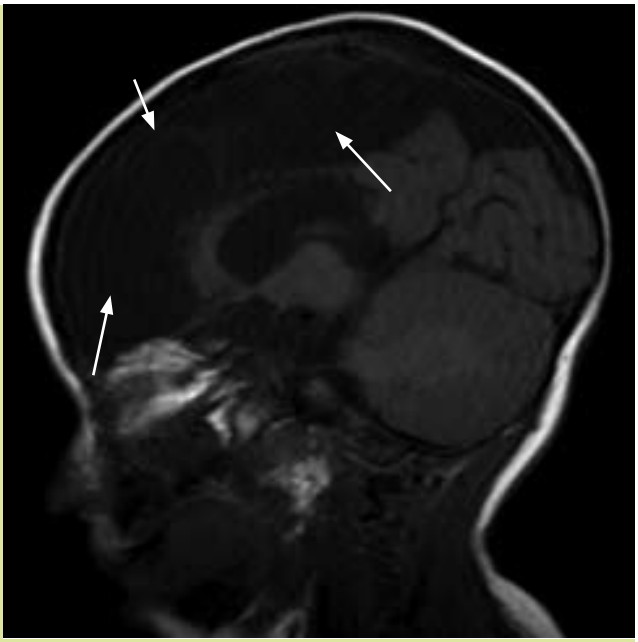
For Aidan Von Gunten, the road to recovery has consumed the majority of his young life. Now 2 years old, Aidan still continues with his weekly rehabilitation sessions and wears a brace on his left foot. His mom describes him as “a very happy, typical kid who is above his age level in everything except self-help and motor skills, and those deficits are only a couple of months off.”

Although the reported incidence and prevalence of pediatric stroke have increased over the past two decades, it has been a struggle for physicians to obtain sufficient data because so little information has been made available. A smattering of medical centers across the United States have established pediatric stroke registries, but the data lack consistency and no system was established for compiling, analyzing and sharing that data.

But all of that is changing now, on both a statewide and international basis. Last summer, the Ohio Pediatric Stroke Registry, which received its first-year funding through a $22,000 Cleveland Clinic research grant, expanded beyond the Cleveland Clinic Children’s Hospital to include six other children’s hospitals in Ohio. Two more Ohio children’s hospitals are expected to participate as well. The statewide nature of this Web-based registry makes it the first of its kind in the nation.

Dr. Friedman sees this collaborative initiative not only as a logical outgrowth and expansion of Cleveland Clinic as a leading stroke center for adults – Cleveland Clinic was certified as a Primary Stroke Center by the Joint Commission on Accreditation of Healthcare Organizations in early 2005 – but also as necessary on so many other levels, including providing a solid basis for ongoing research into the causes, treatment and outcome of pediatric stroke. The collaboration also is necessary, he says, to compete for grant funding alongside more well-recognized areas of pediatric research that have held the edge.

“If you consider that the conservative estimate of childhood stroke is around double that of pediatric brain tumors, the discrepancy in peer-reviewed funding agencies’ support of pediatric stroke becomes apparent,” he says. “The aftereffects of pediatric stroke can last a lifetime. Considering the physical problems survivors may face and the financial impact of that upon society, it makes economic sense to make every effort to advance the prevention and treatment of pediatric stroke.”



Side view showing extensive damage (arrows) to an infant brain after a complete left middle cerebral artery stroke.

"If you consider that the conservative estimate of childhood stroke is around double that of pediatric brain tumors, the discrepancy in peer-reviewed funding agencies' support of pediatric stroke becomes apparent." Neil Friedman, M.B., Ch.B.

The establishment of the pediatric stroke registry already has made a difference: the registry's data are being included in the International Pediatric Stroke Study Consortium (IPSS). Initiated in 2003, the IPSS has been collecting data from 61 centers spanning 17 countries, including the U.S., Canada, Italy, Australia and China. The objective of the IPSS is to study ischemic stroke risk factors, treatments and outcomes, and to develop standardized protocols for diagnosis, investigation of risk factors and specific therapies.

"Such an international consortium on this scale is unheard of," says Dr. Friedman. "If we can work together successfully on this, it may allow us all to continue taking part in other studies and open so many more doors in researching and treating pediatric stroke and other pediatric diseases." ◘

To hear a podcast with Dr. Friedman, go to clevelandclinic.org/clevelandclinicmagazine.

Is Your Child at Risk?

Pediatric stroke strikes more than six in every 100,000 children each year, according to numerous recent studies. Although up to one-third of pediatric strokes have an unknown cause, Cleveland Clinic pediatric neurologist Neil Friedman, M.B., Ch.B., points to a number of underlying causes that can put a child at risk for a stroke:

- **congenital heart disease**
- **blood clotting disorders**
- **viral infections, such as chicken pox**
- **sickle cell disease**
- **blood vessel disorders, such as dissection, moyamoya disease, vasculitis and neurofibromatosis**

Certain populations of children have increased risk of stroke. For example, African-American children with sickle cell disease (SCD) are twice as likely to have an outright or silent stroke compared to healthy children. Called such because they don't offer the classic symptoms of stroke, silent strokes still cause real damage to the brain, affecting cognitive, memory, motor and language skills. The STOP trial (Stroke Prevention in Sickle Cell Anemia), which involved periodic blood transfusions in SCD patients with significant vessel narrowing to lower their hemoglobin S levels to below 30 percent, showed a 92 percent reduction of stroke in that group, compared with standard therapy, according to Dr. Friedman.

Asian children, too, have an increased risk of stroke from moyamoya disease, a vascular disease in which blood vessels are displaced on the brain. Moyamoya means "puff of smoke" in Japanese and refers to the clump of abnormal blood vessels that forms as a result of the blockage. These children can benefit from neurosurgery, Dr. Friedman explains, "to move blood vessels from outside the brain to inside the brain."

Watch for these Signs

Common symptoms of childhood stroke include:

- seizures
- weakness or paralysis on one side of the body
- severe headache
- difficulty speaking or slurred speech
- severe and long-lasting nausea or vomiting for no apparent reason
- blurred vision or vision loss
- loss of balance, difficulty walking

IF YOU SUSPECT STROKE, CALL 9-1-1 IMMEDIATELY.

Giving Today for Better Healthcare

TOMORROW

Cleveland Clinic receives $70 million gift for the new Arnold and Sydell Miller Family Pavilion

"Our family has always been proud to say that Cleveland is our home," says Sydell Miller. "It's important for us to plant seeds for the future by giving back to our community today."

Last fall, Mrs. Miller and her daughters, Lauren Spilman and Stacie Halpern, did just that. They donated $70 million to Cleveland Clinic, making it one of the largest gifts in the philanthropic history of the United States.

The gift will name the new Arnold and Sydell Miller Family Pavilion. In addition to becoming the Clinic's main gateway, the pavilion will contain a large outpatient facility, a hospital tower and state-of-the-art technology building. The programs within these buildings will promote the most advanced practices and technologies in the prevention, diagnosis and treatment of heart disease.

Sydell Miller

Mrs. Miller notes, "This gift is a way for our family to honor the memory of my husband, Arnold M. Miller, as a true entrepreneur. We feel that this gift will continue the entrepreneurial spirit of Cleveland Clinic with its innovation and leadership in healthcare."

ENTREPRENEURS TOGETHER

Arnold and Sydell Miller were married in 1958. While working together in their beauty salon, Mrs. Miller began retail selling accessories. She then opened the first women's specialty sportswear store, called "Tops-N-Bottoms." Several years later, the Millers developed Ardell, an innovative manufacturer of individual eyelashes.

In 1980 the Millers co-founded Matrix Essentials, Inc. As the hair care company grew, Mrs. Miller realized that beauty did not stop at the hairline and added skin care, cosmetics, body care and sun care products to the company's popular hair care and hair color lines. In addition, Mrs. Miller helped salons realize the value of providing a total one-stop beauty experience through her novel "day spa" concept.

When Mr. Miller passed away in 1992, Mrs. Miller continued at the helm, running Matrix and doubling the company's sales. That same year, however, she also faced a personal crisis, undergoing emergency heart bypass surgery at Cleveland Clinic. Through her own care and experiences, Mrs. Miller came to befriend her heart surgeon, Delos M. Cosgrove, M.D., now Chief Executive Officer and President of Cleveland Clinic, and staff cardiologist, Mehdi Razavi, M.D.

> "It's important for us to plant seeds for the future by giving back to our community today." *Sydell Miller*

TIME TO PURSUE PHILANTHROPIC GOALS

In 1994, Mrs. Miller orchestrated the sale of Matrix Essentials to Bristol-Myers. Since her retirement in 1996, she has concentrated her energy and spirit on her family, as well as directing her philanthropic interests through the Arnold and Sydell Miller Family Foundation.

Referring to her family's recent gift to Cleveland Clinic, Mrs. Miller comments, "I've experienced firsthand Cleveland Clinic's tradition of world-class patient care. Our gift will help the Clinic continue that practice and extend its long history of healthcare innovations. It will enable other patients to experience lifesaving care and improve the quality of life for all people...today and in the future."

A Good Philanthropic

INVESTMENT

Bienes gift supports urological institute

As certified public accountants, Michael and Dianne Bienes probably have a better than average grasp of what constitutes a good investment. So when Mr. Bienes characterizes the couple's gift to the Cleveland Clinic Glickman Urological Institute as "the best investment of a million dollars I ever made," he knows what he's talking about.

Both native New Yorkers, the Bieneses relocated to Ft. Lauderdale, Fla., in 1974, where they continued their accountancy practice and where Mr. Bienes managed an investment fund until retiring in 1992 while still in his 50s. Inveterate lovers of the arts, the Bieneses have enjoyed dividing their time for the past 18 years between Ft. Lauderdale and the cultural riches of London, England, with occasional trips to Italy.

> "We're put on this earth to help each other, especially in matters of health."
>
> *Michael Bienes*

MEDICAL ROAD LEADS TO CLEVELAND CLINIC

The Bieneses' path never crossed with Cleveland Clinic until 2004, when Mr. Bienes' Florida cardiologist detected several large cysts on his kidney. "She wanted me to have the very best, and so she contacted Andy Novick at Cleveland Clinic," Mr. Bienes explains.

Dr. Novick, Chairman of the Cleveland Clinic Glickman Urological Institute and world-renowned for his expertise in complex kidney surgeries, confirmed that Mr. Bienes would need to have the cyst surgically removed.

The Bieneses traveled to Cleveland so that Dr. Novick could perform the delicate operation. They were impressed with Dr. Novick's dedication to excellence at their first meeting, Mr. Bienes recalls. "As soon as we met Dr. Andy, his commitment was obvious."

Dr. Novick successfully removed the cyst, and Mr. Bienes spent several days recovering at Cleveland Clinic with Mrs. Bienes close by at the InterContinental Hotel. During their stay, the Bieneses learned about the plans for constructing the Glickman Tower, future home of the Glickman Urological Institute. Mr. Bienes says, "My wife told me, 'You can't say no to supporting it.'"

GENEROUS GIVING FOR HEALTH, ARTS, EDUCATION

That generous response is typical of his beloved wife of 32 years, Mr. Bienes says with pride. "She is the one who taught me how to give. She doesn't just talk the talk, she walks the walk."

With Mrs. Bienes as guide, the couple quietly supports an amazing array of groups, including several fine arts organizations in London. In Broward County, Fla., where Ft. Lauderdale is located, they have built the Bienes Center for the Literary Arts. In addition, they are helping to construct a new African-American Research Center at the county library, providing annual scholarships to the 22 Catholic schools in the archdiocese and building a theater at a local Catholic high school.

Cognizant of the need to be good stewards of their resources, the Bieneses consider every philanthropic decision with great care. "We never dreamed we would have this measure of success. The Lord has been good to us," Mr. Bienes says. "We believe we are blessed and that we should give back."

Mr. and Mrs. Bienes credit Dr. Novick as the catalyst for their gift to the Glickman Urological Institute, which was a departure from their usual philanthropic focus on the arts and education. But they also feel strongly that Cleveland Clinic's core mission meshes with their philosophy of life. "It's another thing my wife has taught me," Mr. Bienes says. "We're put on this earth to help each other, especially in matters of health. That's life – the most important thing in this world."

In Loving Memory and

GOOD HEALTH

Allens give $2 million toward new Heart and Vascular Institute

To Richard (R.E.) Allen, life is a precious gift that is not to be taken lightly. Today, the resident of Stuart, Fla., says he's grateful to be alive, thanks to Cleveland Clinic Chief Executive Officer and President Delos M. Cosgrove, M.D., who performed a heart valve replacement on Mr. Allen in 1998 to fix a heart murmur.

R.E. and Beverly Allen

"My experience with Cleveland Clinic has always been excellent," says Mr. Allen who recently gave a generous gift of $2 million toward Cleveland Clinic's new Heart and Vascular Institute. "Cleveland Clinic was instrumental in saving my

life. We wanted to contribute to the institute as a way to further promote good health, not just for ourselves, but for many people for generations to come."

> "Our fondest wish is that these healing professionals will have the facilities and technology they need to prevent heart disease. Forever."
>
> *R.E. Allen*

HONORING JOAN ALLEN

The gift also was given to honor Mr. Allen's first wife, Joan, who died of lung cancer in 1990. The late Mrs. Allen was the accountant for Imperial Cup Corporation, the company she and Mr. Allen founded in Kenton, Ohio.

Joan Allen

"Our hope is that this gift, given in memory of Joan, will support Cleveland Clinic doctors in the critical work of helping patients and discovering new treatments for heart disease," notes Mr. Allen. "Our fondest wish is that these healing professionals will have the facilities and technology they need to prevent heart disease. Forever."

Before the sale of Imperial Cup to Federal Paperboard in 1990, Mr. Allen served as chief executive officer of the large manufacturer of paper and plastic cups. Today, Mr. Allen is active in Allen Investments, a firm he established following the sale of Imperial Cup.

STAYING ACTIVE AND HEALTHY

Mr. and Mrs. Allen, who have been married for eight years, believe that the secret to staying healthy and young is staying active. In their spare time, the Allens enjoy hunting, fishing and traveling. In early December, they hunt on their 167-acre farm in northwestern Ohio, and in the spring and summer they fish their five-acre lake.

Mrs. Allen, who takes pride in preparing the game that they hunt, has had a passion for cooking for many years, publishing her first cookbook, called *Go Go Gourmet*, in the early 1970s. Since then, she has written three more cookbooks.

Currently, Mrs. Allen focuses on creating healthy cuisine that is infused with home-grown herbs from her gardens in Florida and Ohio. Along with eating healthier, the Allens exercise about five days a week for 45 minutes on a treadmill or stationary bicycle. Mrs. Allen, who began exercising in 1982, says, "R.E. started exercising in 1966, and now he's 85. But he acts and looks 60. I'll be 70 in two years and I think that exercising and a good diet really keep us healthy and young at heart."

In addition to their generous gift, the Allens also support Cleveland Clinic as members of the Heart and Vascular Institute Leadership Board. "We are proud to be a part of the Cleveland Clinic family," says Mrs. Allen. "We work hard to keep ourselves healthy, but we are thankful that this incredible institution is around to help us should we need it again."

Keeping A PROMISE

Schey Foundation's gift creates Center for Advanced Cognitive Function

For years, Ralph Schey has been intrigued by the mysteries of memory, wondering why some people become senile, while others don't, and what can be done to delay or stop senility from settling in.

"For as long as I've known him, he's been fascinated by this topic," marvels his wife, Luci, who has been married to the retired chief executive officer and chairman of the board of Scott Fetzer Company for 21 years. "He's read books and books about memory."

Ralph and Luci Schey

As evidence of the Scheys' continuing interest in the topic, they recently gave a generous gift of $2 million to create the Center for Advanced Cognitive Function, funded by the Ralph and Luci Schey Foundation. Dedicated enthusiasts of world-class healthcare, the Scheys have given several million dollars to support Cleveland Clinic over the years.

The Center for Advanced Cognitive Function currently is being coordinated by Richard Rudick, M.D., Director of the Cleveland Clinic's Mellen Center for Multiple Sclerosis Treatment and Research. The center, which will be housed in the Department of Neurology's Mellen Center, will conduct research designed to lead to better treatments for patients with such conditions as Parkinson's, Alzheimer's, multiple sclerosis and epilepsy. It also will offer comprehensive educational and support services for patients and their caretakers.

> "When I was 4 years old, my mother taught me it's important to give back to the world more than you take from it."
>
> *Ralph Schey*

Currently a member of Cleveland Clinic's Board of Trustees, Mr. Schey is a longtime Cleveland Clinic philanthropist. His giving focuses primarily on the fields of healthcare and education, because he desires to help people lead healthier and more fulfilling lives. "I'm a big believer in the Clinic," he notes, "because of its cutting-edge research, innovations in healthcare and intellectual curiosity. These are valuable traits for an institution that will lead us to better medicine and healthcare."

The Scheys, who in earlier times traveled the world together for business and pleasure, are committed to giving back to a world that has rewarded them so richly. Both are dedicated volunteers. Mrs. Schey, an avid golfer and curler, is passionate about the arts. She serves on the board of trustees of the Cleveland Orchestra, as well as the boards of the Cleveland Play House and Playhouse Square. Most recently, Mr. Schey served on the Ohio Board of Regents, the boards of trustees of Ohio University and the Ohio University Foundation, and the board of directors of the Harvard Business School.

When Mr. Schey is asked about his philosophy of giving, his gaze shifts to the distance. "When I was 4 years old, my mother taught me it's important to give back to the world more than you take from it," he says softly. "That's something I've carried with me my entire life."

Years later, when he was shipping out to serve in the 249th Combat Engineering Batallion of the Army Corps of Engineers in World War II, he recalls making a promise to God. As he left the New York Harbor, he said, "If I come back alive, I promise to make the world a better place." He smiles, "And I'm a man who keeps his promise."

Ensuring the Future of Medicine

You can help ensure the future of medicine by supporting the world-class patient care, research and education that has made Cleveland Clinic one of America's best hospitals. As a not-for-profit academic medical center, we depend on the philanthropic support of people like you. Every gift, no matter how large or small, makes a difference in the lives of our patients.

For more information about giving to Cleveland Clinic, visit us online at **clevelandclinic.org/giving**.

Reducing More Than Weight

Philip Schauer, M.D., Director of Advanced Laparoscopic and Bariatric Surgery, Cleveland Clinic Bariatric and Metabolic Institute, answers questions about weight loss surgery.

Sixty-six out of every 100 people are overweight, and 60 million Americans are classified as obese. Overweight and obese people are more likely than people of average weight to develop Type 2 diabetes, fatty liver disease, sleep apnea, high cholesterol, gallbladder disease and kidney disease, as well as cardiovascular diseases and cancer.

For severely overweight people, weight loss surgery can help them reclaim their life and their health.

Why is bariatric surgery more successful than dieting or weight loss medications?

For most people, dieting yields temporary results. And while weight loss medications work, they are only modestly effective. On average, people lose only about 10 to 15 pounds while on the medications. Bariatric surgery currently is the only effective method to achieve significant, long-term weight loss. Most patients lose from 50 to 70 percent of their excess weight, depending on the bariatric procedure they receive. And the pounds usually stay off.

Is bariatric surgery an option for all overweight people?

Generally, bariatric surgery is for people who are 100 pounds or more overweight and have obesity-related medical conditions. It's not for someone who wants to lose 30 pounds or who wants to look good for a beach vacation. Candidates for bariatric surgery must be between the ages of 18 and 60 and have a Body Mass Index [BMI] of 40 or greater. Patients in this age range with a BMI between 35 and 40 also are candidates if they have obesity-related conditions such as Type 2 diabetes or hypertension. Carefully selected older patients and adolescents also can benefit significantly from bariatric surgery.

How does bariatric surgery work?

Weight loss surgery does one of three things: shrinks the stomach, shortens the digestive tract [small intestine or bowel], or combines these two therapies. With smaller stomachs, people eat less; and with shorter intestines, they digest less. Shrinking the stomach is called restrictive surgery, and shortening the small intestine is known as malabsorption, because a shortened intestine can't absorb as many calories and nutrients.

To shrink the stomach, surgeons separate a small part of the upper stomach from the rest of the organ either by stapling it into a pouch shape or by wrapping a constrictive or laparoscopic band around it to form an open-ended pouch. This pouch, which is stapled to the esophagus [food pipe], becomes the patient's functional stomach. To achieve malabsorption, the surgeon bypasses part of the small intestine where most digestion occurs.

The most common bariatric procedure performed in the United States, and at Cleveland Clinic, is the Roux-en-Y gastric bypass, which is the combination approach mentioned earlier. More than 95 percent of our bariatric surgery patients undergo the Roux-en-Y gastric bypass procedure using minimally invasive surgical techniques.

Does bariatric surgery cure weight-related diseases?

Resolution or improvement of obesity-related conditions is dramatic after bariatric surgery. No other medical or surgical intervention simultaneously treats as many diseases as bariatric surgery does. (See graphic, right.)

Diabetes traditionally has been viewed as a condition without a cure that gradually worsens. We want doctors to see bariatric surgery as a treatment – and a likely cure – for Type 2 diabetes. One-third of diabetic patients discontinue their medication immediately after surgery, even before weight loss. The other two-thirds of patients experience steady improvement, so that within a year after surgery, 83 percent of patients no longer have diabetes.

What risks are associated with bariatric surgery?

Overall, the risks of bariatric surgery are fewer than those related to obesity. All patients run the risk of nutritional deficiencies after surgery, including iron deficiency, vitamin B-12 deficiency and fat-soluble vitamin deficiencies. But these deficiencies are preventable or easily managed with regular monitoring and routine supplementation with multivitamins, iron and calcium.

Anastomotic leaks [a leak at the juncture of the pouch and the esophagus] are a serious complication after Roux-en-Y gastric bypass and can lead to peritonitis. The rate at which leaks occur at Cleveland Clinic is currently less than 5 percent. Leaks are checked at the end of each surgery by flooding the suture line between the pouch and esophagus with water. It's like checking the inner tube of a bicycle tire for leaks: you look for air bubbles. Precautions also are taken to help detect and drain leaks that may arise after surgery. If a major leak is discovered, the patient needs to return to the operating table.

Gallstones develop in about 30 percent of patients within a few months after bariatric surgery because of rapid weight loss. Many surgeons remove the gallbladder during bariatric surgery to prevent patients from developing gallstones. To reduce the incidence of gallstones, we give patients a medication manufactured from naturally made bile salts.

Other possible complications arising from a Roux-en-Y gastric bypass include blood clots, internal hernias, small bowel obstruction, marginal ulcers, pancreatitis, esophagitis and malnutrition. About 0.2 percent of patients suffer blood clotting after Roux-en-Y. To prevent clots, patients are given blood thinners and are required to walk the day after surgery to ensure healthy circulation in their legs.

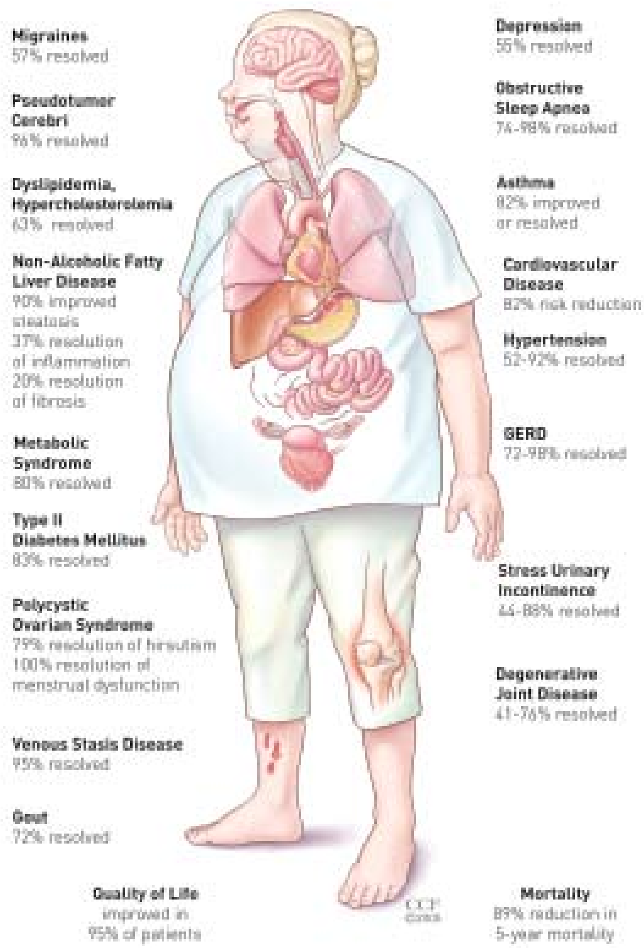
What's the future of bariatric surgery?

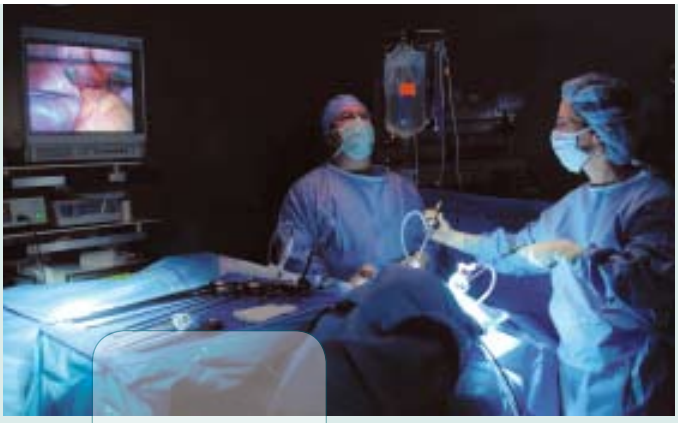
In five to 10 years, I believe that bariatric surgery will be performed without incisions, using an endoscope inserted through the patient's mouth. This approach will dramatically reduce pain and recovery time. Patients may be able to go home the same day and back to work the day after the procedure.

Though still early in development, advances in endoscopic stitching and stapling may allow surgeons to create stomach pouches from inside the body, without having to make an incision. Other technology on the horizon includes the use of tubes or stents placed directly in the duodenum [the first part of the small intestine] and intragastric balloons placed in the stomach to serve as a temporary pouch. Another promising advance involves implanting a device into the intestines or stomach that can send an electric current into the duodenum to stimulate the feeling of fullness.

To read more about the benefits of weight loss and current research, go to clevelandclinic.org/clevelandclinicmagazine.

Losing to Win





A Small Approach to a Big Problem

Joanne Carr still remembers her painful periods. The agonizing episodes turned her life upside down for two weeks each month, at times leaving her bedfast. Since her menstrual cycles were irregular, Carr was never quite sure when the gnawing aches would begin, bringing her busy life to a halt.

"I had many different types of procedures to relieve the pain, but nothing worked. The breaking point came last year when the pain got so bad I had to be admitted to the hospital," says Carr, a 50-year-old wife, mother of two and a department director for a South Florida city.

A computed tomography (CT) scan revealed the source of her distress: uterine fibroids, and many of them. Freedom from pain would require a hysterectomy. Still, an active Carr was hesitant to undergo a surgery from which it would take six weeks to recover.

Carr was weighing the decision between the benefits of living pain-free and the inconvenience of a long recovery associated with traditional hysterectomy when a co-worker gave her a newspaper article on laparoscopic hysterectomy.

Above: Stephen Zimberg, M.D., and Viviane Connor, M.D.

Hope came alive. She made an appointment with Stephen Zimberg, M.D., Co-director of Minimally Invasive Gynecology at Cleveland Clinic Florida, to discuss her options. "Dr. Zimberg told me he could make me feel better, and he certainly did," she says in a relieved tone.

Like Carr, about 600,000 women undergo hysterectomies annually and uterine fibroids account for nearly 30 percent of the cases, according to the American College of Obstetrics and Gynecologists. Uterine cancer and ovarian cysts also are common reasons. About 65 percent of hysterectomies are abdominal procedures, which require a six-inch-long incision and a six-week, often painful, recovery.

Alternatively, laparoscopic hysterectomies require only three incisions – each about the size of a fingernail – around the navel, explains Dr. Zimberg's colleague, Viviane Connor, M.D. The chief benefit is a recovery period of only seven to 10 days. Decreased blood loss, lower risk of infection and post-operative fevers, and less chance of blood clots forming in the patient's legs are among the other major advantages.

Most women considering a hysterectomy are candidates for the laparoscopic procedure, according to Dr. Zimberg. He reports that about 97 percent of the hysterectomies he and Dr. Connor perform are approached laparoscopically. The small percentage of remaining women are unable to benefit from the new technology because their uterus is too large or they have known cancers. However, Drs. Zimberg and Connor are working to increase the number of women who can benefit from laparoscopic hysterectomies.

"We have been developing some of the skills to deal with endometrial cancers laparoscopically," Dr. Zimberg says. "We are also able to remove uteruses up to the size of a five- or six-month pregnancy, which is very large. Our patients go home the same afternoon or the next morning and are back to work within a week."

Drs. Zimberg and Connor have been performing the procedure since July 2003, handling between five and eight laparoscopic hysterectomies each week. During that time they have found no additional patient risks with the new technology. "The risk associated with laparoscopic hysterectomies is the same as with open cases except for a slight risk of blood vessel injuries," says Dr. Zimberg. "With laparoscopic procedures of any kind, inadvertent blood vessel injuries can result from the instruments used during surgery." These injuries, however, are rare in the hands of experienced laparoscopic surgeons, according to studies conducted by the Swiss Association for Laparoscopic and Thoracoscopic Surgery.

Despite the advantages of a laparoscopic hysterectomy, the majority of hysterectomies are still performed using an abdominal incision simply because many doctors are not qualified to perform the newer procedure. For one, surgeons must invest in learning the laparoscopic technique, and they must have operating rooms that are equipped with the necessary devices. Two, insurance reimbursement is about the same for both laparoscopic and traditional hysterectomies, thus lowering the appeal even further for surgeons to learn the minimally invasive approach.

For patients like Joanne Carr, the decision for a laparoscopic procedure was a simple one, and Dr. Zimberg expects physicians to get more pressure from patients to learn these new techniques in the coming years. Seeing laparoscopic hysterectomies become the mainstream approach rather than the minority choice, he adds, is merely a matter of patient education.

"If surgery can be a pleasure, this was quite a pleasure," Carr says, noting that her painful periods are becoming a distant memory. "The recovery was relatively painless. I took some Advil at home but, by the third day, I was moving around the house taking care of things. It has improved my quality of life 100 percent."

Faced with Hysterectomy?

If you are faced with hysterectomy and are considering the laparoscopic method, be sure to ask your gynecologist:

1) how many procedures he or she has performed; and

2) what his or her rate of conversion to a traditional approach is.

Keep in mind that, even if a laparoscopic method is planned, your surgeon may have to convert to the traditional procedure if there are unexpected findings, such as cancer.

Beyond understanding the basics of the procedure, along with the benefits and the recovery time, the conversion question is the most important one you can ask your gynecologist.

CLINICAL TRIALS

Bringing Innovation Down to Earth

Technology developed as part of the "Star Wars" defense program is being studied at the Cleveland Clinic Taussig Cancer Center for use in a battle much more immediate and closer to home: the fight against breast cancer. Investigators are testing the BioScanIR System, a dynamic infrared imaging tool that uses an ultra-sensitive sensor developed at NASA's Jet Propulsion Laboratory. Because the sensor may detect minute temperature changes associated with breast tumors, BioScanIR may offer significant improvement in monitoring the effectiveness of pre-surgical therapy for breast cancer patients.

The study aims to discover how sensitive and specific the technology is in measuring tumor response to therapy and how it compares with other means of assessing treatment. Results so far appear promising, says Suzanne R. Fanning, D.O., a fellow in hematology and medical oncology and coordinator of the study.

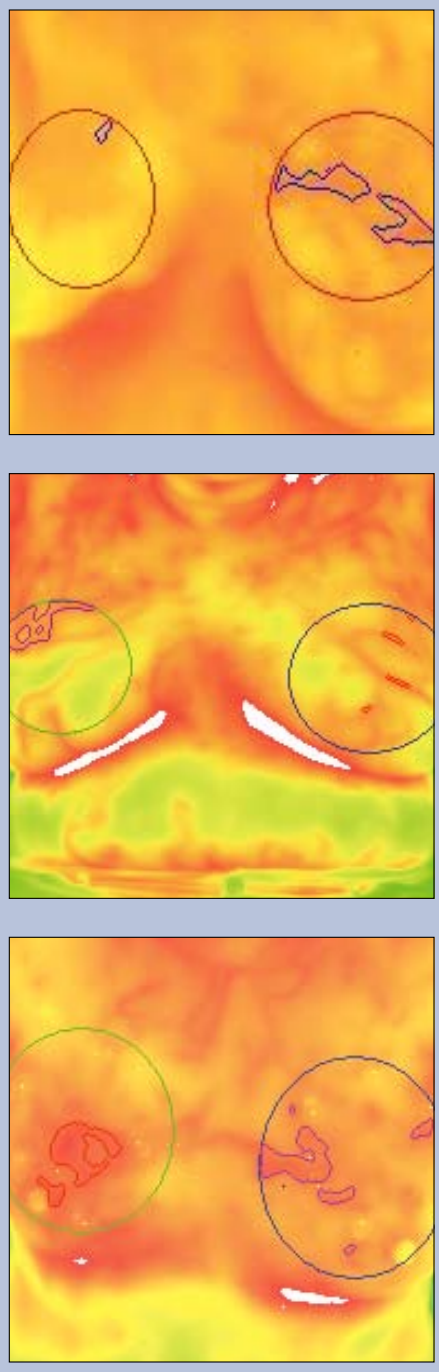
Typically, patients with locally advanced breast cancer undergo chemotherapy or hormonal therapy to shrink their tumors before surgery. Progress is gauged by repeated physical exams during treatment. Biopsies, mammograms, ultrasound, magnetic resonance imaging (MRI) and positron emission tomography (PET) also are used but generally only at initial diagnosis and right before surgery.

These current measures, however, can be imprecise, expensive and painful, and may involve exposure to radiation, says David E. Weng, M.D., Ph.D., the study's principal investigator. BioScanIR, he says, "has none of those disadvantages."

BioScanIR would enable doctors to evaluate tumor response during therapy and, if necessary, adjust treatment accordingly. A high-resolution image can be taken in less than 30 seconds and, in the future, results will be immediate through the system's software, notes Dr. Fanning. The BioScanIR system also is portable; it can be brought right to the patient.

The advantages don't stop there.The BioScanIR system may have other applications, Dr. Weng says. Among them, a possible pain-free alternative or supplement to mammograms. BioScanIR might also prove useful in vascular, cardiovascular and cosmetic surgery, and has potential applications to other tumors, such as melanoma, he adds.

For more information about the BioScanIR clinical trial, contact Suzanne Fanning, D.O., at 216.444.8375.



A dynamic infrared imaging tool, known as the BioScanIR System, uses an ultra-sensitive sensor to detect minute temperature changes associated with breast tumors. The circled areas, called "regions of interest," highlight changes in blood flow that indicate tumor response to therapy. Researchers hope the tool will allow them to evaluate tumor response to pre-surgical therapy and, if necessary, adjust treatment accordingly.

Images courtesy of Advanced BioPhotonics, Incorporated.

Taking Pain Relief to Heart

Steven E. Nissen, M.D., is on a mission to find answers for a major health issue: whether or not pain relievers are safe for millions of arthritis patients who also have heart disease.

Dr. Nissen, a cardiologist, is the lead investigator of the first worldwide clinical trial to study three of the most commonly used pain relievers: ibuprofen (Motrin), naproxen (Naprosyn or Aleve) and celecoxib (Celebrex), commonly known as COX-2 inhibitors (or coxibs) and nonsteroidal anti-inflammatory drugs (NSAIDS). When the study is complete in four years, researchers expect to be able to determine the safety of these drugs, which have received much public attention recently for their potential link to cardiovascular conditions.

"Every day, patients who have arthritis and heart disease come in to see their doctors, but the doctors don't know what to give their patients," Dr. Nissen says. "We need answers, and this research is going to help us find those answers."

Dr. Nissen and his colleagues first suggested that COX-2 medications had the potential to cause heart disease and stroke in an article published in the *Journal of the American Medical Association* in 2001.

"There has never been a trial study done on these pain relievers for arthritis patients with heart disease or patients with multiple risk factors for developing heart disease," says Dr. Nissen, who also is President of the American College of Cardiology, the professional society representing 33,000 cardiovascular specialists. "All prior clinical trials on these drugs have been done on arthritis patients, but they did not have heart disease or their risk for heart disease was low. Unfortunately, that doesn't tell us much."

The study, which will include about 20,000 patients from the United States, Canada, South America, Europe and Australia, has been named the PRECISION trial – Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen or Naproxen. The study will enroll patients with osteoarthritis, the most common form of arthritis, who have heart disease or who have multiple risk factors for heart disease. Some patients with rheumatoid arthritis also will be recruited for the study, which is expected to launch by mid-2006.

Although Pfizer Inc., makers of Celebrex, will fund the PRECISION trial – estimated to cost more than $100 million – Dr. Nissen stressed the leadership and conduct of the trial will be directed independently by the Cleveland Clinic Cardiovascular Coordinating Center. What's more, an executive committee consisting of leaders in cardiovascular medicine, rheumatology and gastroenterology, including a staff member from the National Heart, Lung, and Blood Institute of the National Institutes of Health, will govern the trial.

"The study leadership will insist that none of the members of the executive committee accepts honoraria or any other compensation from makers of any drugs in this class," says Dr. Nissen. "We recognize the importance of conducting this trial according to the highest standards of integrity."

Removing Sox to Prevent Disease

Molecular biologist Veronique Lefebvre, Ph.D., is researching whether two genes involved in cartilage formation may lead to new treatments for osteoarthritis, a disease that afflicts one in three American adults and is the nation's leading cause of disability.

In 2001, Dr. Lefebvre's research team discovered that two genes, Sox5 and Sox6, are required to form the cartilage structures that progressively change into bone as we grow. By the time we're adults, we are left with only a thin layer of cartilage that covers and protects the ends of bones in joints. This cartilage acts like a cushion or shock absorber, allowing us to move without pain and without damaging bone. But as we age, this cartilage often degenerates and the bones rub together, causing pain and restricting movement.

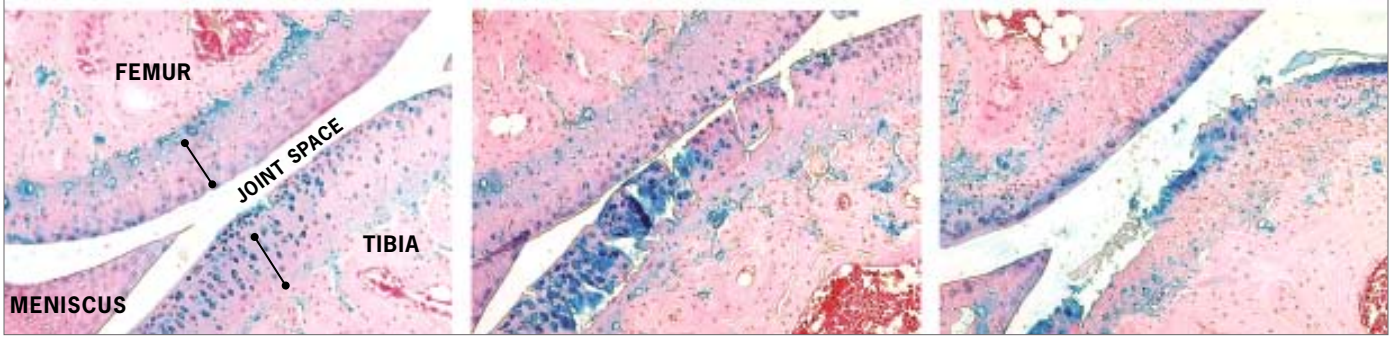
"The research project under way now is to understand what these genes do as we age," says Dr. Lefebvre. "After birth, we have cartilage in our joints that helps us move easily. As we age, most of us lose or damage our cartilage. Why and how this happens, however, is poorly understood."

Dr. Lefebvre's research team is generating models that don't have the Sox5 and Sox6 genes to see how quickly joint cartilage is lost and if osteoarthritis is an end result. Dr. Lefebvre also hopes to find out how these genes make cartilage and whether these genes are essential to preserving cartilage.

"It's clear that when people reach 70 years of age, the majority have osteoarthritis because of the degeneration of cartilage," she says, theorizing that the genes may become idle as we age.

If the research proves the Sox5 and Sox6 genes are essential for healthy cartilage, Dr. Lefebvre says a new drug could be developed to restart the genes to maintain or restore cartilage.

From left to right: Progressive degeneration of articular cartilage (double lines), the hallmark of human osteoarthritis, is seen in the knees of a model with this disease. In the far right image, the articular cartilage is essentially gone.



The Flow Must Go On

Peripheral arterial disease (PAD) is a common circulatory problem in which the arteries supplying blood to legs or arms become clogged or partially blocked. PAD affects 10 million people in the United States, including 5 percent who are older than 50.

While PAD often can be treated with exercise, a low-fat diet and medication to reduce cholesterol, some PAD patients need bypass surgery. Typically, surgeons take a vein to bypass the blocked artery in the leg, but when a vein is not available, a synthetic tube or prosthetic graft is used.

The problem with synthetic grafts is that tissue builds up at connection points, which eventually causes them to fail. Cleveland Clinic vascular surgeon Linda Graham, M.D., received a $1.9 million grant from the National Institutes of Health to find out what triggers this tissue growth.

Old Tropical Infection Drug is New Anti-Tumor Hope

For decades, sodium stibogluconate (SSG) has been used by doctors to cure patients with tropical parasitic infections. Now Cleveland Clinic researchers are investigating whether SSG can be used to kill life-threatening tumors.

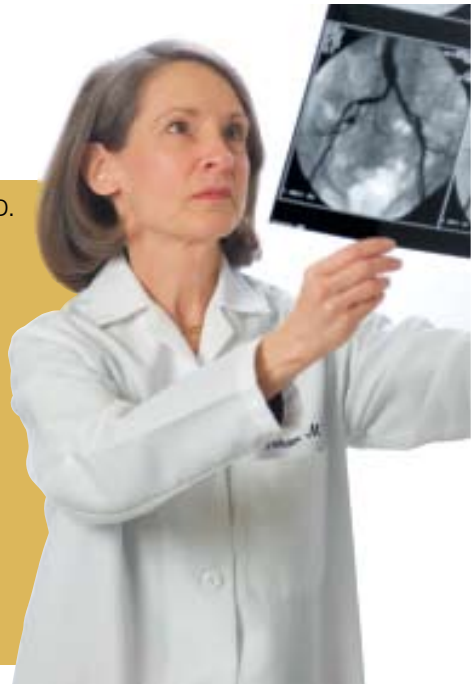
"Several years ago, SSG was on a list of compounds that we wanted to test for anticancer properties," says cancer research biologist Taolin Yi, Ph.D. "Among the various molecules we screened, we found one in SSG that was active in killing cancer cells. It was surprising."

In laboratory experiments, Dr. Yi and his research team showed that the compound is effective in battling solid tumors, such as melanoma and kidney cancer, and lymphoma and myeloma.

An additional exciting element about SSG is that doctors already know the compound, despite its tremendous potency, is well-tolerated by humans. Most chemicals that show anticancer capacities go through rigorous toxicity tests and other experiments that may take five years or more to complete. Ninety percent of these chemicals are eliminated during the toxicity study phase. But when a chemical is determined to be safe, a small Phase I human clinical trial begins and lasts for about a year.

"SSG has been used in humans for more than 50 years, so we know that it's safe," Dr. Yi says. "We discovered SSG's anticancer properties in 2002 and began recruiting patients in 2005 for Phase I trials. That's amazingly fast." If Phase I trials show promising results, SSG will be required to undergo Phase II and Phase III human trials that usually take up to five years to complete.

This discovery is exciting because the drug is so well-tolerated and seemingly effective. "Most of the chemicals we test show only a partial blockage of tumor growth or may slow down tumor growth. In our test models, SSG eliminated the tumor," says Dr. Yi. "That's rare."



Linda Graham, M.D.

"One of the things we have found in our research so far is the lipids [fats], particularly lipids that are oxidized, tend to amass more in the prosthetic grafts," says Dr. Graham. "These oxidized lipids cause some of the cells to function abnormally, which, in turn, causes cells to produce excess scar tissue.

"Through our research, we are trying to determine the cellular mechanism that causes cells to produce the excess scar tissue," Dr. Graham says. "After we learn why this occurs, we can develop new treatments to inhibit the buildup of scar tissue."

Managing Multiple Medications

In living longer, we are bound to encounter more risks. But most of us don't think that taking more than one medication or repeating a medicine can be a health hazard. However, as multiple medications are more commonly prescribed for individuals, the risks associated with this "polypharmacy" increase, particularly among older adults. In fact, the results of a nine-year study published in the December 2004 issue of the *Journal of the American Geriatrics Society* showed that the most common reason elderly patients were hospitalized for adverse drug reactions was polypharmacy.

Polypharmacy has become more common within the past 20 years because of the development of newer, safer drugs and the aging of the population. Literally, the term describes the use of multiple medications in a single person to manage or treat one or more conditions or diseases. "But popular use of the term polypharmacy now includes the undesirable effects of multiple medications taken in inappropriate doses or in doses inappropriate for the older person," says Robert M. Palmer, M.D., Section Head of Geriatric Medicine.

Taking multiple medications to treat health concerns often is necessary. "However, drugs can counteract each other, thereby neutralizing any intended benefit," Dr. Palmer says. Two or more drugs can produce similar side effects, thus increasing the risk of unwanted side effects. Some drugs can either enhance or diminish the positive effects of another drug.

Risks for Older Adults

The body's ability to metabolize drugs may change or diminish as it ages, making it unable to excrete normal adult dosages of medication. Over time, a buildup of certain drugs could cause toxicity. Demerol (meperidine), for example, is a narcotic often given by injection to patients who have acute and severe pain, especially after surgery. One product (metabolite) of Demerol has toxic effects within the body. The process of eliminating Demerol from the body can be delayed further by lessened kidney function because of age or kidney disease. Giving an older adult repeated doses of Demerol can cause toxic levels of the drug's metabolite to build up in the body. Such high levels of the drug can cause seizures or delirium.

Some drugs, when used in combination, can worsen existing conditions. For example, someone who is taking a prescription medication for an overactive bladder may not think twice about buying an over-the-counter antihistamine to relieve allergy symptoms. But if that person also has a memory problem or early-stage dementia, the result of mixing these two drugs could be acute confusion and disorientation.

Gaining Benefits, Reducing Risks

"Appropriate polypharmacy," as Dr. Palmer calls it, is essential to treating certain types of conditions, such as heart or renal failure. It is possible to safely manage an older adult's health with the use of multiple medications, but the responsibility falls on both the patient and the doctor.

"Medications should not be prescribed unless there is a clear indication for them and only if the benefits of taking the medication outweigh the risks," states Dr. Palmer. Doctors also must be very cautious in determining the correct dosage of medication for an older adult.

A list called the "Beers Criteria for Potentially Inappropriate Medication Use in Older Adults" was developed to serve as a reference tool for doctors. This list includes drugs that have not been proven effective, have been proven effective but have extreme negative effects or are only appropriate in certain circumstances. The list can be found online at the Archives of Internal Medicine Web site at archinternmed.com (type "Beers Criteria" in the search box).

Dr. Palmer advises patients not to take any over-the-counter medications, herbal remedies or megavitamins without first discussing it with their doctor. And because most of us now have more than one doctor, he advises people to keep all their doctors informed of all of the medications they have been prescribed.

Perhaps most important in regard to polypharmacy, "When a new symptom occurs when you are not acutely ill," Dr. Palmer says, "you should suspect an adverse drug event and report it to your physician right away."

Tips for Safe Medication Usage

FOLLOW THE TIPS BELOW TO HELP PREVENT A BAD MIX OF MEDICATION

1. Make sure your healthcare providers are aware of ALL the medications you are taking – this includes over-the-counter medications, herbal remedies and vitamins.
2. Know your drug and food allergies.
3. Make a list of your medications and dosages. Keep this with you and update it as necessary.
4. Take your medications exactly as prescribed by your doctor. Do not stop taking your medications unless you talk to your doctor first.
5. Use one pharmacy if possible.

These are general guidelines. Be sure to ask your doctor or pharmacist for guidelines specific to your medications.

The Double Switch

In the summer of 2005, Neal and Julia Freeland of Seattle, Washington, discovered that their soon-to-be-born daughter, Amelia, had several serious heart defects that threatened her life. The following story contains excerpts from Neal's Web log, or blog (http://spaces.msn.com/members/nealfreeland), describing the Freelands' journey into the world of pediatric heart surgery. These excerpts were reprinted with the Freelands' permission.

Pediatric heart surgeon Roger B.B. Mee, who performed Amelia's operation, retired in December 2005 after 37 years of practice. Amelia was one of his last patients.

July 19

Amelia Rose Freeland was born last night ... .

August 17

Amelia's heart is like a wind-up toy. At her birth, we were afraid the whole thing, once on its own and free of the umbilical cord's steady guidance, would spin too rapidly and blow apart. Fortunately, that didn't happen ... Now, the question is "how fast is it winding down?" After our two-week check-up ... the answer seems to be "fairly quickly" ... .

September 19

Amelia is dying ... she's been taking a maximum dosage of two diuretic medicines to shed extra moisture, but still her breathing is difficult, which can be seen in the soft bobbing of her head. Though we've been fortifying her breast milk with formula, her labored breathing is using up the majority of her caloric intake, and she hasn't gained weight for over two weeks. The irony is that even as her heart fails the rest of her body grows. She's gained several inches in length, stretching her weight over a longer frame and making her deep blue eyes her defining feature. Full of curiosity, they engage the world with an imploring sparkle, asking, "what's going on?" As her father, I also see her faint fear and hear her gentle request: "help me."

The procedure she needs is called the double switch. The first switch is to correct the blood supply from the heart to the lungs and body. Currently, the left ventricle supplies blood to the lungs through the pulmonary artery, and the right ventricle to the body through the aorta. This is backwards. Since it's not possible to change the position of the ventricles inside the heart, the solution is to swap the arteries ... .

Amelia's heart is only the size of her little fist, which is an unthinkably small space for the surgeon to operate. It's like sewing wet tissue inside a matchbox ... .

While it's clear that Amelia needs the double switch, the timing of her surgery is in question ... Dr. Mee believes that Amelia should receive the double switch when she is only 3-4 months old (she's 2 now) and sees no benefit in the preliminary band procedure recommended by our doctors in Seattle ... .

October 9

We're off to Cleveland tomorrow morning. As the surgery draws nearer, Julia asks me how I can be so relatively calm and confident knowing Amelia is facing a risky surgery that could end her life. I look at this the other way around – this is the surgery that will save her life. Here's why:

While stationed in Pearl Harbor with the Navy, I learned that Hawaiians traditionally wait until their child's first birthday to cut their hair. They believe this helps ward off the many threats that can end an infant's life. In the developed world, we've mostly forgotten about these risks as medicine has

pushed them back from the forefront of our lives ... . So while Amelia has a rare combination of heart defects and the surgery she is going to experience this week is difficult and risky, I am very comfortable with the odds. Instead of a 95 percent chance of death, she now has a 95 percent chance of life. This surgery is an example of our medical system working, and I am thankful for it. In fact, the only question in my mind right now is, "how long will her hair grow in one year?"

October 12

a tricky heart meets
the lord's hands –
my daughter's breath on my cheek

October 13

As I sat in the waiting room today during Amelia's surgery I thought about how I'll never own a van Gogh painting. I'm just not driven to seek enough money to be able to buy one of these masterpieces, even though I greatly admire them.

But I am driven to do everything I can for Amelia. This was why we came to Cleveland, to put her in the hands of this master surgeon. Even if I were Bill Gates, this would still be exactly the place I would have chosen to have her receive this procedure.

Last week, Dr. Mee announced his retirement. Amelia ... gets one of the last works from an old master, which is a priceless thing. I wonder how I got to be so lucky to help make this happen.

October 15

In the vernacular of his native New Zealand, Dr. Mee judges that Amelia's recovery is going just "fair to middling." She's very young to have undergone such difficult and long surgery, and her body is taking extra time to recover.

October 17

Amelia had a second surgery today to implant a small pacemaker. The generator, about the size of a silver dollar, is in her left abdomen and the lead is attached to her ventricle. The pacemaker is needed to regulate the electrical signal that tells the ventricle muscle to contract. Because her heart developed backwards, the fine, winnowy material that conducts the electrical signal is twisted and possibly broken. It works only intermittently and totally stopped during her first surgery. The good news is that for now her heart seems to have full conduction, so the pacemaker is only a backup. But the conduction system is behaving like an old lamp with a finicky power cord – move it around a bit and the bulb could go out at any moment. It's a good thing to have the pacemaker standing by if needed.

Amelia gets one of the last works from an old master, which is a priceless thing.

October 21

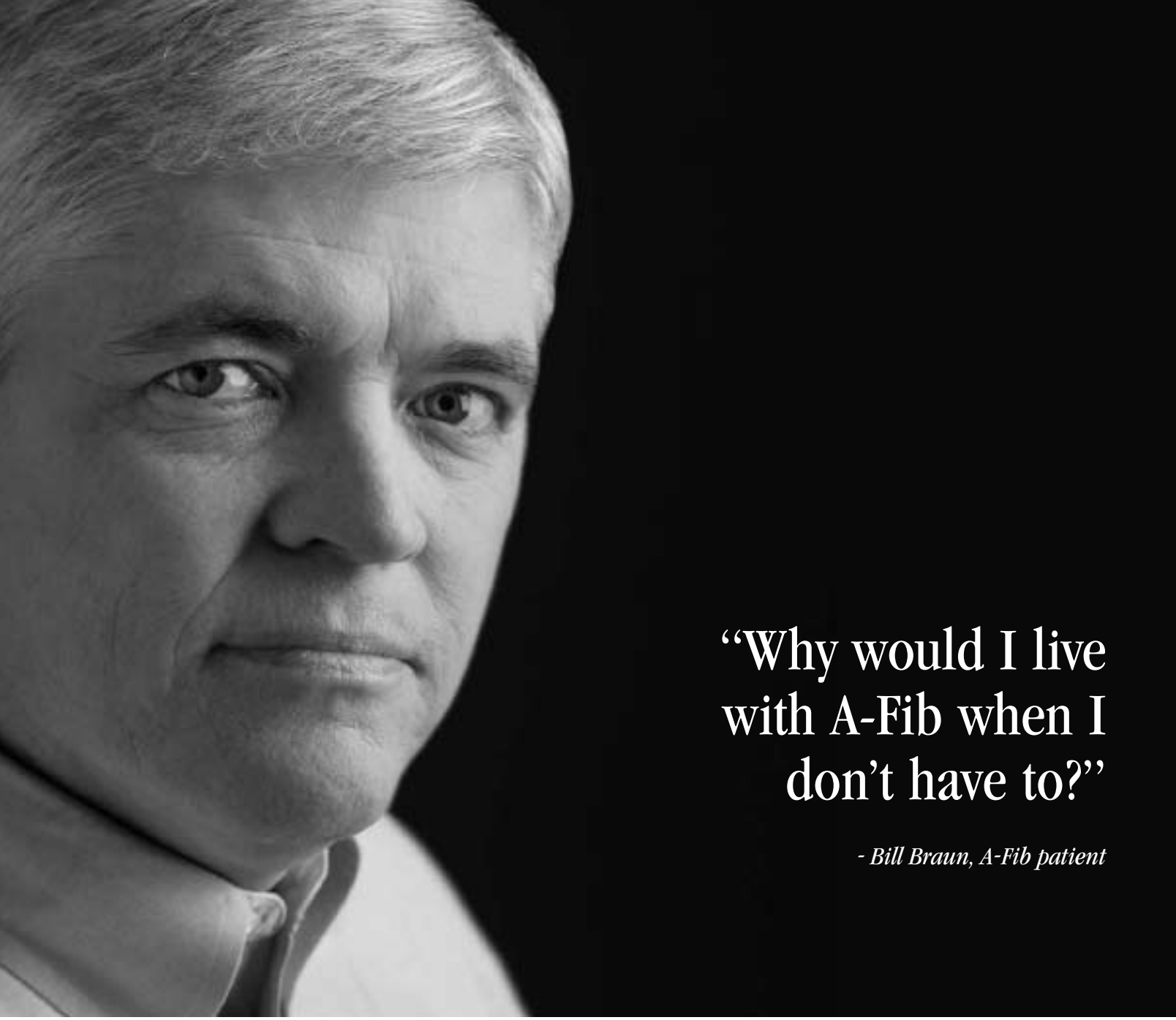
Amelia is doing well ... . Over the last two days the nurses have removed five intravenous lines, two external pacemaker wires, one big toe oxygen sensor, and the nasal oxygen supply tube. She is down to just her heart rate monitor wires and has shifted from 12 medicines fed via infusion machines, to just three taken orally. She has fought back strongly against a pretty virulent bacterial infection, mastered her recovery pain, cleared her gut (I changed 11 diapers today), and found a whole bunch of reasons to keep me up with her tonight. In other words, life is awesome!

October 26

We are out of the hospital. Amelia's final echocardiogram showed a well-functioning heart, with the technician muttering "nice," "really great" and "wow" each time she took a look from a different angle. This was the same technician who didn't utter a single comment on the preoperative echo 13 days ago, and just looked grim as she moved quickly through the process.

October 29

So that's it. We're home and Amelia is doing well. Though we've got a lifetime of hospital check-ups in front of us to monitor her repairs, tricuspid valve and pacemaker, I think this is the end of the beginning. It's been a longer than normal birth story, but I'm thankful for the result.



The Cleveland Clinic has more experience correcting atrial fibrillation than anywhere else in the country. Including ablation and minimally invasive techniques. Not surprising when you consider it's been named the #1 heart center in the nation for eleven years running.

For free advice and to request an informative brochure, call Cleveland Clinic Heart and Vascular Institute at 800/890-2467

Cleveland Clinic

U.S. News AMERICA'S BEST HOSPITALS 2005

The future of healthcare is in your hands.

TODAY'S INNOVATIONS → TOMORROW'S HEALTHCARE

Campaign for Cleveland Clinic

This philanthropic campaign will raise $1.25 billion for

- → expanded world-class facilities
- → groundbreaking research
- → advanced medical education
- → compassionate patient care

Support Cleveland Clinic.

For information, go to: clevelandclinic.org/giving
or call: 216.444.1245 or 800.223.2273 x1245

iSupport
Make a gift online

Cleveland Clinic

The Cleveland Clinic Foundation
Office of Development/UA20
9500 Euclid Avenue, Cleveland, OH 44195

Non-Profit Org.
U.S. Postage
PAID
Cleveland, Ohio
Permit No. 4184