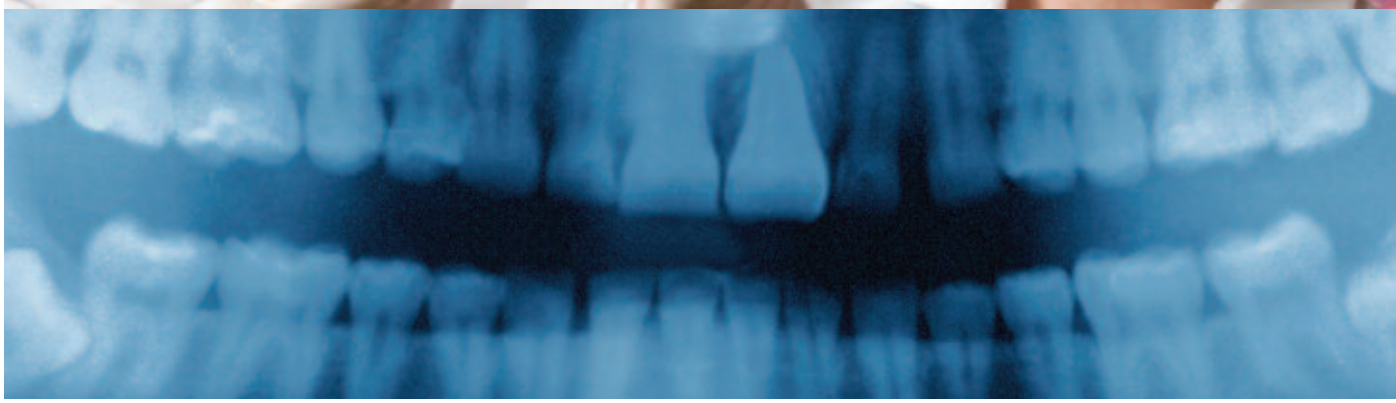
Healthy Healing

BILL WIEGAND



BY ALISA ZAPP MACHALEK

Perhaps you've never noticed, but people don't have scars in their mouths.

If you bite your tongue or the inside of your cheek, it heals without a trace. Even after serious injuries or major surgery, oral scars are very faint. That's in stark contrast to the tough, pinkish bands left elsewhere on the body by nasty bike spills or unsuccessful fence-climbing efforts.

Why is that? And, if somebody could figure it out, could we do away with scars altogether?

Luisa Ann DiPietro asks these questions every day.

And of all people, she is well suited for studies in and around the mouth. Before she became a scientist, DiPietro worked as a dentist.

Precocious Puzzlers

DiPietro, who runs a lab at the University of Illinois at Chicago College of Dentistry, says she was always drawn to math and science. Her father, a math professor, and her late mother, a librarian, both loved to learn new things.

"I grew up in an environment where it was fun to stretch your brain," she says.

DiPietro and her three siblings especially enjoyed math puzzles introduced by their father. A particular favorite involved birthday candles.

On your birthday, DiPietro explains, the number of candles on your cake wouldn't be your age in base 10, but in another base. You'd have to figure out which one.

"We *loved* this," she says. "We never realized how weird it was until my brother brought over his girlfriend." The girlfriend wasn't quite so intrigued with the game, and she declined to participate when her birthday came around, DiPietro remembers.

Like DiPietro, her siblings are still doing science and math.

Her younger brother is a software expert at Sun Microsystems; her sister is a food chemist at Dreyer's ice cream company; and her older brother, a veterinarian, is vice president of the Institute of Agriculture at the University of Tennessee in Knoxville. All four still like puzzles.

Meanwhile, DiPietro's father, now 86, teaches one math course every semester at nearby Eastern Illinois University in Charleston, even though he officially retired about 20 years ago.

▲ Growing up, DiPietro and her siblings played math puzzles with birthday candles.

Healing Under the Microscope

Today, DiPietro studies wound healing in slippery tissues called mucous membranes that protect body openings. Found along the inside of the nose, ears, mouth, and other body cavities, these tissues heal more quickly and with much less scarring than skin.

DiPietro wants to learn how they do it.

She compares the healing of mouth and skin wounds to find the cellular and molecular differences between the two processes. In one approach, she grows human skin and mouth cells in separate plastic dishes to examine how each type responds when scraped and injured by a glass tube.

In another type of experiment, she compares the healing of tiny wounds on the tongues and backs of mice. She also works together with researchers who do similar kinds of experiments with rabbits and human volunteers.

"The long-term goal of my research is to find therapies that will improve healing for people—to turn wound healing into a more rapid, regenerative process," she says.

Specifically, she's trying to help reduce scarring in those with extensive injuries and to speed healing in the 1 million or more Americans whose wounds heal slowly or incompletely, such as people with diabetes or vascular disease.

Research Calling

By the time she graduated from high school, DiPietro knew she was good at science, but she did not have a specific career track in mind. She enrolled at the University of Illinois at Urbana-Champaign, just 60 miles from her childhood home.

During her early years in college, she spent a lot of time considering possible career paths, which included biology, biochemistry, and even sociology.

Then one day, as a junior, she noticed a flyer on a bulletin board outside her academic advisor's office. It described a summer research opportunity sponsored by the American Dental Association.

"I grew up in an environment where it was fun to stretch your brain."

On a whim, DiPietro applied, and she was accepted.

That summer, she got her first taste of research. She used biochemical techniques like mass spectrometry and liquid chromatography to examine whether the chemicals used to make dentures alter cholesterol levels in a person's blood.

It was a great fit. DiPietro liked applying the fine-detail skill of her hands—sharpened during hours of embroidery, sewing, and needlepoint—toward work that she knew might help people someday. She decided to become a dentist.

After dental school, DiPietro completed a 1-year, hands-on training program in general dentistry at Michael Reese Hospital and Medical Center in Chicago. There, she worked alongside a select group of physicians, dentists, and medical and dental residents.

In the emergency room, she treated dental abscesses, replaced lost teeth, sewed up cut lips, and examined patients with facial trauma. In the clinic, she cared for patients whose conditions complicated their dental therapy, including those with cancer of the mouth or cerebral palsy.

▲ DiPietro started out as a dentist.

DiPietro saw how enthralled her colleagues were about the work. The harder the case, the more they liked it. But DiPietro didn't feel the same passion.

"Follow your heart."

She instead called up memories of a unique—and in hindsight, life-changing—class she had taken in dental school years before.

Rather than focusing on a textbook or syllabus, this class relied solely on research publications. The students read a mix of classic scientific papers and recently published ones, then discussed their strengths and weaknesses in class.

Through this exercise, DiPietro learned how to ask scientific questions, design experiments, interpret data, and formulate theories to explain research results—just about everything a scientist does on a daily basis.

"I felt my eyes were literally opened," DiPietro says.

Looking back, she knew that the course had done much more than teach her about biology: It had convinced her to become a researcher. She went back to school to get a Ph.D.

Body, Heal Thyself

Say you nick yourself shaving or rip open your leg skateboarding. Immediately, you feel pain and see blood. Your body kicks into high gear, sandbagging the wound, stretching a protein scaffold over it, and calling in teams of immune system cells that starts a process called inflammation.

The first cells on the scene are neutrophils, which swallow bacteria, then self-destruct by triggering an internal chain reaction of toxic chemicals. Macrophages clean up the remaining debris. Mast cells cause swelling, warmth, and redness.

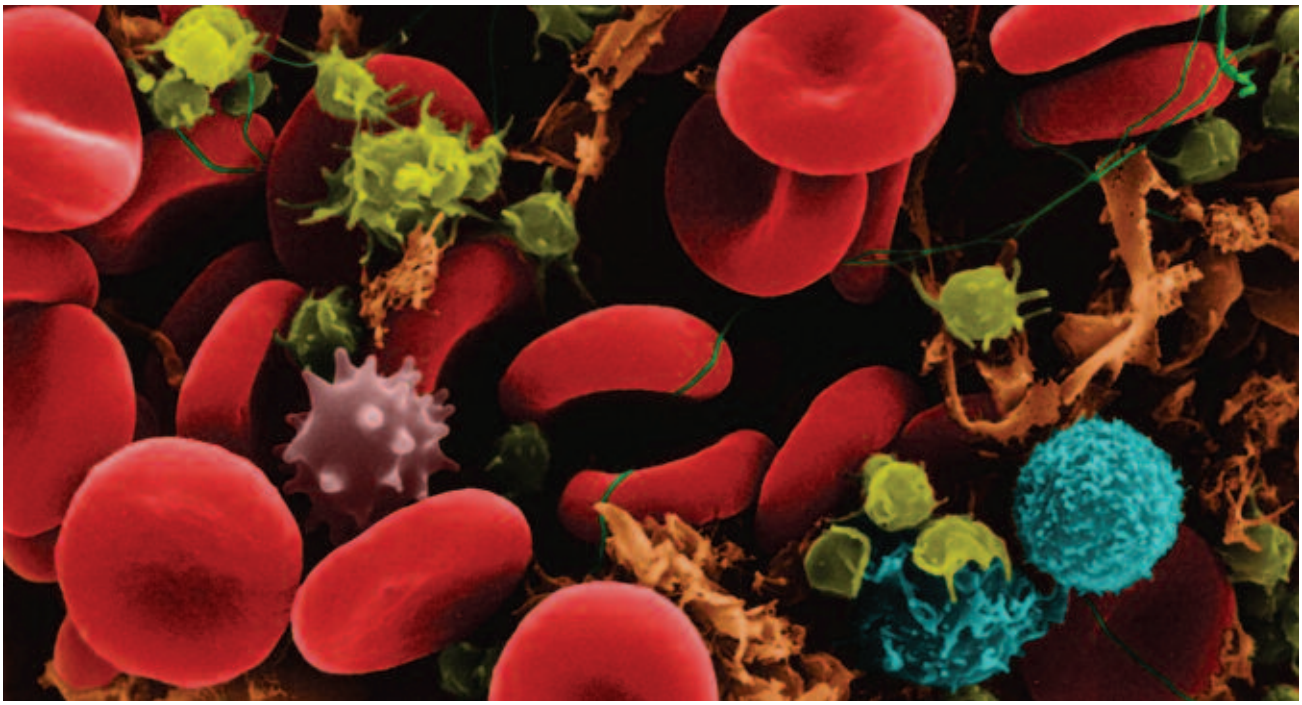
All three cell types release powerful chemical messages that summon even more immune system cells to the damaged site.

As this inflammatory phase of wound healing dies down, the next step—called proliferation—powers up. Cells on the inner surface of blood vessels grow leglike appendages and crawl across the wound, ribboning the area with new vessels that bring needed oxygen and nutrients.

This process, called angiogenesis, can dramatically increase the number of blood vessels in the area.

Eventually, cells around the edges of the injury pull up their roots and crawl over each other to fill in the open wound. Ropelike proteins grab the wound's edges and pull them closed like drawstrings. Finally, the area is draped with a sturdy protein mesh, and the new blood vessels, now no longer needed, die off.

During this amazing series of events, our bodies use thousands of molecules and more than a dozen cell types to heal a wound.



▲ To heal wounds, our bodies use a large collection of cell types, proteins, and molecules.

Too Much of a Good Thing?

The fast and furious burst of inflammation at the beginning of the wound healing process has an important purpose: It protects us against death by microorganisms. Without it, a paper cut or torn hangnail could be potentially fatal!

According to DiPietro, most wounds require some level of inflammation to clean themselves up. But in its enthusiasm to decontaminate wounds, the body turns on inflammation full blast. That's usually more than necessary to sterilize the site.

Excess inflammation often damages healthy, neighboring tissues. This happens when neutrophils spill their caustic, bacteria-killing cocktail, which—believe it or not—includes hydrogen peroxide and the body's version of chlorine bleach.

High levels of inflammation are also linked to disfiguring scars, DiPietro has found. Such scars affect more than a person's appearance and self-esteem—they can impair the use of certain body parts, locking down joints and limbs. If they involve vital internal organs, these scars can be life-threatening.

Together, DiPietro's findings, along with those of other researchers, point to a major shift in thinking about the role of inflammation in wound healing.

In the past, inflammation was considered the vital first step in healing. Now, scientists think that it might not always be a good thing—or rather, it may be too much of a good thing.

"That's been a big surprise," DiPietro says. "It's incredibly exciting to me to be part of this shift in our understanding of healing."

▲ Injuries caused by accidents or surgery leave scars.

Blood Vessels Gone Wild

DiPietro has also found that the body may go overboard with angiogenesis.

Mouth tissues, which heal quickly and without scarring, grow only enough blood vessels to replace those lost due to injury. Once the area has a normal number of vessels, angiogenesis stops, says DiPietro.

But in skin wounds, she explains, the number of vessels increases by up to 10 times—way more than necessary. Most of the excess vessels die off, and the number of blood vessels in the area eventually returns to what it was before the injury.

DiPietro's research suggests that this creates an unintended effect: When healing includes this massive growth of extra blood vessels, it usually leaves a scar.

But it's still not clear what's going on, she says. Does angiogenesis itself promote scarring? Or is it the molecule that triggers angiogenesis? Or the cells that produce the signal? And so on.

DiPietro has begun to address those questions too. The answers may change the way doctors treat cuts, puncture wounds, and burns. She is excited and hopeful that her research will lead to new treatments.

"I hope that in my scientific lifetime, I'll see some of those," she says. "Very few researchers get to take their discovery [to patients]. I hope I'm one of them."

▲ Monthly lunches in DiPietro's office often include exotic ethnic foods.

Leading By Example

DiPietro knows that science is an ongoing, group effort and that each researcher relies on graduate students, postdoctoral fellows, technicians, and other scientists.

DiPietro's concern for her team is legendary. When graduate students choose which professor to work for, many are drawn to her lab.

"She's one of the best mentors I've ever seen—absolutely outstanding," says Aimee Burns, who was DiPietro's lab manager for 9 years.

DiPietro regularly meets one-on-one with each person in her lab. Students describe walking into her office in despair over a failed experiment, then marching out beaming with a new, positive outlook on their research.

She also shepherds a diverse group of a dozen or so workers into a cohesive team. Those in her laboratory come from four continents. They include a mixed group of high school students, undergraduates, graduate students, postdoctoral fellows, medical students and residents, physicians, and volunteers.

Informal gatherings in the lab have been a big hit with her crew.

"At first, [DiPietro] was in a 9-by-9-foot office, and after one of her promotions, she moved to a bigger one," Burns says.

"She didn't know what to make of it, so she decided we should have a monthly potluck lunch in there!"

DiPietro also actively tries to increase the number of underrepresented minorities in research and clinical work.

Before moving to the University of Illinois at Chicago last year, DiPietro was a researcher for nearly 15 years at nearby Loyola University School of Medicine. There, she established a Diversity Scholars program that provides substantial support for

minority medical students to perform a short research project or take a clinical elective.

Perhaps unknowingly, she's also a role model for young women in science. They see, through her example, that it's possible to balance a family and a career in science (see sidebar, right).

"She's very committed to her family without having it take away from her work—and vice-versa," says Megan Schrementi, who was a graduate student in DiPietro's lab for 4 years.

"As a woman in science who would like to have a family, that's something I look up to."

DiPietro has the same advice for any students trying to figure out who they want to be when they grow up.

"Follow your heart. Look for your passion and what interests you—don't let anyone talk you out of that." she says.

DiPietro has certainly taken her own advice.

"To have a job where you're paid to think about things and to learn all the time—I still feel like I have to pinch myself sometimes." ■

A Balancing Act

"My most interesting life experience has been raising twin sons while maintaining my scientific career," says Luisa DiPietro, a wound healing researcher at the University of Illinois at Chicago (see main story). Now 18, the boys were born a few months before DiPietro finished her Ph.D.

LUISA ANN DIPIETRO

▲ DiPietro's two sons graduated from high school this year.

"Only someone who loves science more than sleep would do such a thing!" she admits.

DiPietro vividly recalls some of the crazy things she's done to simultaneously nurture two growing boys and a blossoming career.

While home on bed rest during the last 7 weeks of her pregnancy, she analyzed the results of experiments.

In a hospital waiting room as one of her 18-month-old sons was having a peanut surgically removed from his lung, she put together a scientific seminar. Watching her high school-age son at a swim meet, she read articles she was preparing to publish.

The unstructured nature of research helped a lot, she says.

"Even though scientists work a lot of hours, it tends to be pretty flexible. I could leave the lab and go to my son's school concert or water polo game," DiPietro says.

Researchers she has worked with over the years credit her talent, hard work, phenomenal organizational skills, and wise career choices.

"She has a stable family in a loving home and a wonderful research [program]," says Peter J. Polverini, dean of the University of Michigan School of Dentistry in Ann Arbor.

"I can't think of a better role model, male or female."—*A.Z.M.*