DAMAGE CONTROL

Inflammation: friend or foe? It may be a leading cause of aging and even skin cancer, but in the right hands, it can turn back the clock.

By Maggie Bullock

[redacted] mega-3 tablets, green tea lattes, antioxidant serums: Chances are, you're already engaged in the fight against inflammation. Medicine's biggest, baddest buzzword gets more headlines than Lindsay Lohan (albeit in different publications). It's the subject of countless studies and theories; the basis of more than one "life-saving" diet (see: Mediterranean, Weil, Perricone); and is, according to one skin care entrepreneur, "the single biggest cause of aging."

On the flip side, inflammation is a large part of why laser resurfacers and acid peels and—according to some experts—even doctor's-best-friend Retin-A actually work. Each of these engineers a small injury that causes skin to repair itself—which it does through inflammation. No one's saying you should break up with your derm or toss your tube of Retin-A, but the conflicting claims give pause: Why is one form of inflammation killing us and the other making us prettier—and how are we supposed to know the difference?

But first, perhaps a better question: What *is* inflammation? That's the funny part. At its core, inflammation is basic biological border control—a very good thing. Whether you cut your finger or get sneezed on by a flu-ridden colleague, your immune system deploys specialized repair cells, including mast cells and macrophages, that signal waves of other cells and chemicals to arrive on the scene. The cascade is not unlike gut-renovating a house: Enzymes demolish the damaged tissue, then other workers come in and build it back up. Finally—ideally—the body senses the job is done and shuts down the process.

How much inflammation each of us has is believed to be partly genetic, but smoking, allergens, UV rays, pollution, and hormones (stress-related cortisol, for one) can provoke more of it. Cells in the skin and intestines, for example, are constantly working to kick out the irritants in everything from Marlboros and Doritos to plain old tap water.

Perhaps because of this constant assault, many experts now believe that our repair machinery can get out of whack, stuck in the "on" setting. Chronic inflammation—the bad stuff—has been linked to cancer, heart disease, and Alzheimer's. In the case of heart attacks, inflammation in the blood vessels can weaken the lining of artery walls and cause fatty deposits, or plaques, to rupture, forming vessel-clogging clots. Autoimmune disorders such as lupus and rheumatoid arthritis are, in fact, prime examples of inflammation gone awry; the body has turned its inflammatory (i.e., immune) response on itself, repeatedly assaulting healthy cells in the joints, nerves, and connective tissues.

Though the basic process is the same throughout the body, all inflammation is not created equal—different kinds give us different sensations. If it's in the brain, we get a headache (hello, hangover); in the liver, stomachache or nausea; in the intestines, upset stomach and cramping. And much of it lurks undercover, an unseen, uninvited guest that we can't feel at all.

But what, you may well be asking, is it doing to my *face*? In skin, high levels of inflammation produce exactly what you picture: the redness—and sometimes pain, itching, and flaking—that anyone who suffers from eczema, psoriasis, or rosacea knows all too well. It's not the infection, per se, that makes these conditions so uncomfortable and unsightly—it's the body's war against them. The condition known as chronic actinic dermatitis, in which badly sun-damaged skin becomes dry, scaly, and itchy? That's inflammation too.

And while clogged pores and built-up oil contribute to the miseries of acne, the condition is also caused by bacteria, which incites—you guessed it—inflammation, sometimes leading to pain and scarring. This can become a particularly vicious circle: Stress also causes inflammation, which leads to acne, which leads to more inflammation, and so on.

But even if your pores are Cate Blanchett–perfect, the day-to-day inflammatory response to pollution, smoke, and UV light is inevitably taking its toll. These irritants unleash free radicals, which attack skin cells' protective membrane, allowing them to become dehydrated; this ushers in molecules that break down collagen and elastin and release toxins, including more free radicals. The result doesn't just show up as redness: It's also part of the spots and wrinkling that we all recognize as aging. "It's an ongoing, everyday process, and it's happening to all of us," says dermatologist Fredric Brandt, MD, who has offices in New York City and Miami.

Just how *many* of our spots and wrinkles this is responsible for is unknown. As for

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the potential magnitude of the role inflammation plays in aging, Joel Gelfand, MD, an assistant professor of dermatology at University of Pennsylvania School of Medicine, points to an extremely rare—and nightmarish—inflammatory condition, acquired cutis laxa, in which skin loses elasticity and hangs in loose folds. "It's a very unusual clinical event," Gelfand says. "But it occurs because inflammation is eating up the elastin, which leads us to believe that inflammation may be a cause of elastin breakdown in the skin. But that's just a hypothesis. We need studies."

The danger isn't just aesthetic. "There is a line of thinking that certain kinds of repeated inflammation can create a nurturing environment for skin cancers," says Kevin Cooper, MD, who chairs the department of dermatology at Case Western Reserve University in Cleveland and was recently recognized by the American Academy of Dermatology for his research on inflammation. "We do know, for instance, that sometimes a wound that doesn't heal and is chronically inflamed can get a skin cancer inside of it. That makes us worry a little bit that chronic or repeated wounds might raise our risk of cancer."

While skin cancer has long been assumed to be caused by the DNA mutations inflicted by UV rays, now researchers wonder how much of the problem is, in fact, the body's self-defense response to the sun—inflammation. A study published last year illustrated the potential of chronic inflammation to help a cancer grow. Scientists at the Lankenau Institute of Medical Research in Philadelphia gave mice a single dose of a carcinogen, then exposed them to a poison ivy derivative twice weekly for 20 weeks. The steady irritation of the poison ivy confused the body's immune response. Therefore, IDO, an enzyme whose job is to shut down the immune response, suppressed the defense troops, allowing precancerous cells to develop into tumors.

Cooper predicts sunscreen will one day have an "immune protection factor" rating, similar to SPF, which will measure a cream's ability to prevent the immune suppression caused by sun exposure. "Is skin cancer the direct effect of UV light on the DNA of the skin? Or is inflammation alone causing it? Probably both," says Washington, DC, dermatologist Tina Alster, MD. "We don't know which one is more important."

All of which leads to the big question: Why on earth would patients pay their dermatologists thousands of dollars just to incite this process?

New York City dermatologist David Orentreich, MD, explains the theory behind these short, sharp bouts of inflammation: "Take the new fractionated CO_2 resurfacing laser. It burns skin in a precise, controlled fashion. But the body responds as it would to any burn, removing the damaged components, sending in workman cells." Due to the nature of the injury, this results in smoother, younger-looking skin instead of an unsightly scar. "Little dots of light make tiny holes in the skin's surface," he says. "The healthy tissue surrounding each of the holes knits back together."

Of course, laser-wielding docs are quick to point out that the inflammation they're causing is short-term—and productive. "You have to separate the chronic inflammation that causes aging from the acute inflammation caused by treatment," Brandt says. "Acute stimulates the skin's repair system, laying down new collagen. But afterward, the white cells in your body issue a termination statement, and it stops."

"You have to do a little bad to get some good," Alster declares. "Right now, there's nothing better than lasers to initiate a new collagen response. There is no topical product that can do that. But the word here is *controlled* injury."

Years ago, doctors would prescribe oral steroids to calm post-treatment redness and irritation. "Over time, we realized the inflammation was actually helping to increase the end benefit," Orentreich says. "Maybe we should do less to quench it." Now, for the sake of patient comfort and convenience—after all, less downtime makes a procedure sound a whole lot more appealing—there's an increased interest in modulating the response without quelling it entirely.

For example, after performing fractionated resurfacing treatments, Brandt regularly pops patients in front of the GentleWaves LED panel of yellow light for 35 seconds. "It calms the inflammation and the activity that breaks down the collagen. You want to wound the skin but shorten the inflammatory cascade," Brandt explains.

Alster recently published a paper in *The Journal of Dermatologic Surgery* detailing a split-face test: Post-Fraxel resurfacing, she flashed only one side of the face with GentleWaves and left the other alone. The GentleWaves-exposed side recovered quickly, with a day or two less swelling and redness. Interestingly, a week later, both halves had the same cosmetic benefit.

But anyone who's tried to camouflage an aggravated, overtreated complexion knows that inflammation isn't just inflicted by high-power laser. What about the irritants in our own bathroom cabinets: rough scrubs and intense peels; harsh, drying cleansers; potent topical treatments? Retin-A (and its fellow prescription retinoids Tazorac, Avage, and Differin) helps lay down new collagen by kick-starting the wound healing process, but it also makes most patients red—at least until skin becomes conditioned to tolerate it. Devotees have been using Retin-A for 37 years; it is a proven antiager and, by regulating cellular turnover, it may have cancer-fighting benefits. But if it works by causing inflammation, wouldn't daily use make that chronic?

Brandt maintains that most products are not inflammatory as long as they're used properly. Common sense comes into play: If something continually makes your face red and irritated, well then, don't use it.

Alster agrees. "People who keep pushing the envelope with inflammation may be doing more harm than good," she says. "When they come into my office looking very red from using Retin-A, I say, 'Well, don't get to that stage. Figure out what works best for you.'"

Like every expert interviewed for this article, Alster argues that there is more evidence in favor of acute inflammatory procedures and creams than there is against them. "We don't know how much inflammation is good and how much is bad—that differs from person to person," she admits. "But saying that anything that causes inflammation is bad for you? That's really going out on a limb."

Still, says Case Western's Cooper: "Will the kind of inflammation that's being created by these [dermatological] procedures be helpful in the long run or could it have a dark side down the line? It's unclear. But it's reasonable to raise the question." ●

Firefighters: Clinique Medical Recovery Week Complex uses one percent hydrocortisone to calm inflammation and vitamin C to minimize hyperpigmentation; Sustainable Youth Technologies Immune Performance Elasticity Cream contains an aloe extract said to minimize the elastin-munching effects of inflammation; the new SKIN1 by Dr. Gram line, including Eye Rescue (shown), centers around 14 proven anti-inflammatories, including green tea extract, chamomile oil, and oat flour; allantoin, a key ingredient in Dr. Brandt Anti-Irritant Soothing Moisturizer, "is like topical aspirin," says Fredric Brandt, MD.

All still lifes: Steven Krause