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## Plumping Up the Volume: Wrinkle Fillers Spur Collagen Production

**New study shows that Restylane injections do more than just temporarily fill in the lines**

Are you always on the hunt for a way to iron out the time lines etched in your face? Behold: a new study has found that multiple injections of Restylane, a popular "skin filler" believed to temporarily zap lines by literally filling them in, actually stimulates the skin to produce collagen, a protein that keeps it firm and supple but dwindles with age and sun exposure causing sagging and wrinkling.

"We found that in addition to filling up space, these injections induce robust production of collagen, thought to give rise to the smooth contour of the skin," says Frank Wang, a clinical research fellow in the dermatology department at the University of Michigan Medical School in Ann Arbor and co-author of the study published in the February issue of *Archives of Dermatology*.

Americans spend millions of dollars annually on plastic surgery and assorted wrinkle busters from Botox (a toxin that temporarily erases facial creases by paralyzing the muscles that cause them) to pricey moisturizers in a desperate attempt to hide any evidence of (gasp!) aging. Injections of dermal fillers—relative newcomers to the wrinkle-fighting arena—have become increasingly popular since the Food and Drug Administration in late 2003 approved the use of Restylane (made by Medicis Pharmaceutical Corp.) to temporarily fill in deep smile lines burrowing from the nose to the mouth.

It is estimated that more than a million Americans annually receive injections of Restylane and other more recently approved dermal fillers like Allergan's Juv?derm and Radiesse (made by BioForm Medical, Inc.). The key ingredient in Restylane is hyaluronic acid, a naturally occurring compound in the skin and connective tissue. The molecules of hyaluronic acid bind to water in the skin, locking in moisture; the loss of it as we age causes the skin to become dehydrated, contributing to crinkles and creases.

Board certified plastic surgeon George Peck, Jr., director of the Peck Center for Cosmetic Surgery in West Orange, N.J., says that while Botox is a favorite for freezing brow furrows and crow's feet, skin fillers are mostly used to plump up smile lines, scars caused by acne and other skin conditions, and aging, thinning lips. The price tag for Restylane ranges from around \$500 to \$750 per syringe, Peck says, adding that the number of doses required depends on the depth of the lines: In many cases, one shot is enough to fill in both smile lines, in others, two syringes may be needed.

He says that the effects of Restylane generally last from four to six months, depending on the patient and where it is injected. (He notes that Restylane replaced less effective collagen injections, which lasted from one to three months and, unlike Restylane, required allergy tests and a 30-day waiting period to rule out reactions.) "We think some of the duration from Restylane is due to this new collagen production," Wang says.

Researchers made their discovery after injecting Restylane chosen because it had been used safely used for several years—into the arms of 11 healthy men and women, ages 64 to 84, who all had visible signs of mild to moderate sun damage. Each volunteer received three injections of 0.7 milliliter of Restylane (spaced two to five centimeters apart) in one forearm and three injections of the same strength of saline (salt water) solution at similar intervals in the other arm.

Scientists then took punch biopsies (pimple-size skin samples) from the injection sites four and 13 weeks later. When they examined the skin plugs, they discovered that the Restylane injections had not only filled in crimps, but had actually stimulated collagen growth in the sun-damaged areas. "We thought we could do this," Wang says, "but we were surprised at the robust level of production of collagen." [see note below]

Researchers believe the injections trigger new collagen growth by stretching fibroblasts (the cells that secrete collagen proteins), prompting them to crank out more collagen as well as by stimulating chemicals that prevent the breakdown of collagen.



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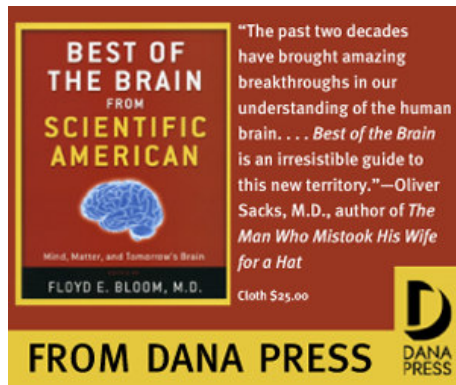
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Wang says that in young, healthy skin, spindle-shaped fibroblasts stretch out and make loads of collagen, which form a strong web that supports the skin and keeps it firm. Alas, during natural and photo aging (caused by the sun's ultraviolet rays), collagen deteriorates and fibroblasts—which cling to it—crumple amid the loose and droopy strands.

According to Wang, researchers were searching for a way to stretch the fibroblasts again to see if that would prompt them to start pumping out healthy amounts of collagen. They thought Restylane might do the trick and when they examined the volunteers' skin samples, discovered that it had: The fibroblasts were taut and there was new collagen production.

So will the findings lead to a brave new world in which eternally unlined, youthful skin is but an injection away?—If only.

"This is exciting news, but it won't dramatically alter the landscape in the long run," says Peck. "Restylane will still be just a quick fix. It's something that someone can just come into the office, lie down, have and then go out to lunch and look better ... It's that quick and that easy. But it won't create enough collagen formation to completely erase nasal-labial folds (lines from the nose to the mouth)."

The bottom line, Peck says: "Eventually, everyone gets wrinkles. Restylane is a nice modality to have for facial rejuvenation—even people who have surgery have nasal-labial folds so even they may want Restylane injections. But Restylane is the icing on the cake—not the cake itself. It won't work forever. Eventually people [bent on the line-free look] have to have plastic surgery, but, even then, wrinkles are a fact of life. You can't change the aging process, but we can make you look better doing it."

*Note: Wang says that the maker of Restylane donated the syringes used in the study but did not participate in, sponsor or know the results of the trial before they were published. He says that researchers cannot vouch for the effects of the other skin fillers on the market, because they use different recipes. Still, expect the news to heat up the already hot competition between rivals Restylane and Juv?derm, which Wang likened to the "war between Coke and Pepsi."*

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