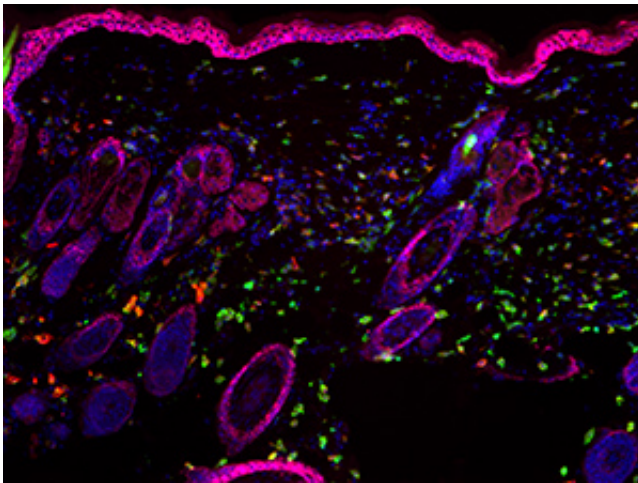


Unusual skin cancer linked to chronic allergy from metal orthopedic implant

October 9 2014, by Michael C. Purdy



Activated immune cells, shown in red and green, cluster at the site of an allergic skin rash. Scientists have learned that this inflammation can promote skin tumor formation if it persists. Credit: S. Demehri, T. Cunningham

In rare cases, patients with allergies to metals develop persistent skin rashes after metal devices are implanted near the skin. New research suggests these patients may be at increased risk of an unusual and aggressive form of skin cancer.

Metal alloys help make orthopedic implants stronger and more durable. But people with sensitivity to these metals, which include nickel, cobalt and chromium, can develop [chronic inflammation](#) that promotes the development of skin cancers, report researchers at Washington

University School of Medicine and Barnes-Jewish Hospital in St. Louis.

The team's findings were published online Oct. 8 in the *Journal of Clinical Investigation*.

The researchers were alerted to the connection by a patient who had surgery at another hospital to have a metal rod implanted to repair a fractured ankle. After the surgery, the patient developed a skin rash on her ankle, near the location of the implant.

The patient turned out to be allergic to nickel in the implant, which led surgeons at the other hospital to remove it. But the rash persisted, and a few years later, a rare form of [skin cancer](#) known as Marjolin's ulcer developed at the surgical site. The cancer, which had become painful and ulcerated, was diagnosed and removed by physicians at Barnes-Jewish Hospital.

The researchers showed in mouse models that chronic skin inflammation caused by continuous skin contact with allergens contributes to tumor development. The finding suggests that [patients](#) with metal implants near the skin may need to be monitored for this type of inflammation, according to the researchers. The results likely also will lead to debate and further research on whether physicians should test for metal sensitivity in patients preparing for surgery to get these types of implants.

Chronic inflammation from metal implants can cause joint pain and swelling and contribute to joint failure. And when these implants are placed near the skin, fewer than 5 percent of patients develop an inflammatory rash related to the implant.

The patient's diagnosis with Marjolin's ulcer, an invasive and potentially deadly [squamous cell cancer](#), surprised physicians. The patient was

under 50 years old, and Marjolin's ulcer is extremely rare in people who are young and otherwise healthy. This type of cancer most often is identified in patients with a previous history of skin cancers, but this patient had never had skin cancer.

To investigate whether inflammation from the implant contributed to the tumor, the researchers studied mouse models of [contact allergy](#).

"A contact allergy is a different kind of reaction from allergies to pollen, pet dander or food," said senior author Wayne M. Yokoyama, MD, a Howard Hughes Medical Institute investigator at the School of Medicine. "A contact allergy usually develops when an allergen touches the skin or is close to it. Skin rash in response to nickel and poison ivy are two common examples of contact allergies."

The researchers showed that contact allergy brings inflammatory cells and molecules to the site of the allergic reaction. If the contact allergen remains a long time – as was the case with the patient's implant – different inflammatory cells and molecules become active at the site of the reaction. The new mix of cells and molecules promotes the development of skin tumors.

"This model supported cancer development so strongly that some mice developed invasive squamous cell skin cancers similar to the patient's tumor," said lead author Shadmehr Demehri, MD, PhD, a dermatologist and postdoctoral fellow.

When the researchers examined the cells and molecules involved in chronic contact allergy in mice, they identified several that already had been linked to tumor development. Some of these cells and molecules also were present in biopsy samples from the patient's ankle. The scientists are working to identify which inflammatory cells and molecules are most supportive of cancer formation.

"If you're allergic to something, the first thing to do is to avoid it, but the patient couldn't," said Yokoyama, the Sam and Audrey Loew Levin Professor of Medicine. "Some nickel had likely seeped from it into her tissue and was still present in her skin even after the implant was removed. It's as if a patient allergic to poison ivy kept putting poison ivy on the skin."

To prevent such adverse events, the researchers suggested that the potential for [allergic reactions](#) to metal implants be assessed in patients who have had the implants and in patients preparing to receive them.

"Allergen-free versions of some implants are available," Demehri said. "These versions may cost more or be less durable, but for some patients with sensitivity to metals, they may be the best option."

Similar to [metal implants](#), some dental restoration materials and tattoo inks contain substances associated with allergic reactions and cancers on the skin or in the mouth. Those clinical observations also could be explained by the new findings. The researchers suggested that the potential for these other allergens to promote [skin](#) cancer needs to be examined further.

More information: Demehri S, Cunningham TJ, Hurst EA, Schaffer A, Sheinbein DM, Yokoyama WM. Chronic allergic contact dermatitis promotes skin cancer. *The Journal of Clinical Investigation*, online Oct. 8, 2014.

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