

Researchers discover new hereditary form of cold-induced urticarial rash

28 April 2020



Credit: CC0 Public Domain

Skin rash combined with head and joint pain are the symptoms that patients with familial (hereditary) cold urticaria develop when exposed to temperatures below 15 °C. Researchers from Charité - Universitätsmedizin Berlin have discovered a new, previously unknown form of this inflammatory skin disorder. In addition to explaining why conventional treatments are ineffective in some people with the disorder, their findings also point to potential alternatives. The results of this research have been published in *Nature Communications*.

In many people, this disorder will develop suddenly, but gradually lessen and disappear again after a number of years. Its cause remains unknown. A small proportion of sufferers inherit the disorder from their parents. In these people, the [immune system response](#) to [cold temperatures](#) is due to a [genetic defect](#) which, in addition to skin rash, causes signs of systemic inflammation, including fever and [joint pain](#). Researchers led by PD Dr. Karoline Krause of the Department of Dermatology, Venereology and Allergology on Campus Charité Mitte have now discovered a new form of cold urticaria which is caused by a

previously unknown mutation in the Factor 12 gene. The name proposed for this new hereditary disorder is Factor XII-associated cold autoinflammatory syndrome, or FACAS.

"Our report relates to several members of the same family seen in our department. At least one person in each generation of this family reported identical symptoms, which they had suffered from birth," explains PD Dr. Krause. "These individuals all developed a burning skin rash after 30 minutes of exposure to temperatures below 15°C (59°F). The rash was exacerbated by windy weather and [humid conditions](#), and only resolved several hours after the individual returned to a warmer room."

The patients also reported other symptoms like chills, fatigue, headache and joint pain. In contrast to people who develop cold urticaria spontaneously, these patients did not respond to a cold provocation test known as the 'ice cube test.' Their symptoms also failed to respond to antihistamines, which are normally an effective treatment for cold urticaria. "The family's symptoms were clearly indicative of a hereditary form of cold urticaria," says the dermatologist. "We therefore studied the affected individual's genetic information, looking for mutations known to cause the disorder's hereditary form, but to no avail. What we found instead was a previously unknown defect in the Factor 12 gene."

The researchers were then able to show that this defect leads to the activation of the contact system pathway, and that the hives are produced as a result of the subsequent release of inflammatory mediators. "Interestingly, defects in the Factor 12 gene had previously been known to cause a very different condition that we refer to as hereditary angioedema," explains PD Dr. Krause. Hereditary angioedema is characterized by sudden attacks of severe and painful swelling in the deeper tissues.

"While the symptoms reported by FACAS patients

are those of hereditary cold urticaria, the underlying mechanisms causing these symptoms are entirely different. These patients therefore qualify for treatment with drugs normally used in hereditary angioedema." Interestingly, one of the FACAS [patients](#) showed an immediate response when given icatibant, a drug normally used to treat acute attacks of [hereditary angioedema](#). Upon administration, the patient's cold-induced symptoms resolved quickly and almost completely.

More information: Jörg Scheffel et al, Cold-induced urticarial autoinflammatory syndrome related to factor XII activation, *Nature Communications* (2020). [DOI: 10.1038/s41467-019-13984-8](#)

Provided by Charité - Universitätsmedizin Berlin

APA citation: Researchers discover new hereditary form of cold-induced urticarial rash (2020, April 28) retrieved 20 October 2020 from <https://medicalxpress.com/news/2020-04-hereditary-cold-induced-urticarial-rash.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.