# A child with severe wrinkling of the skin of the palms

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**Test your diagnostic skills in our regular dermatology quiz. What is the cause of this child's rapid and severe skin wrinkling that affects her palms after exposure to a small amount of water?**

## Case presentation

A 12-year-old girl presents with a lifelong history of rapid severe wrinkling of the skin of her palms after minimal exposure to water. The episodes are asymptomatic and self-resolve within 40 to 60 minutes after drying. Her soles are not affected.

The girl's medical background is unremarkable. Her parents have accepted the palm skin wrinkling as normal for her, but they are concerned about the appearance and wondering if anything can be done about it.

On examination, before water exposure there are no gross abnormalities of the patient's palms or other skin areas. After simple wetting of her palms in a stream of water from a tap her palms promptly wrinkle, with the formation of oedematous whitish plaques and papules (Figure). She does not complain of discomfort, pruritus or pain. After drying, her palms return to normal.

**Figure.** The girl's wrinkled palms after exposure to a stream of tap water.

## Differential diagnoses

This condition is called aquagenic wrinkling of the palms (AWP). Causes to consider include the following.

- **Normal variant.** Wrinkling after prolonged exposure to water is a normal physiological response driven by the intracellular absorption of water and the activation of the sympathetic nervous system, resulting in vasoconstriction and puckering of the above skin layers, which is observed grossly as wrinkling. Normal aquagenic wrinkling typically occurs after about 11 minutes of immersion.[1] The rapidity of this patient's response to a small amount of water suggests other diagnoses should be considered before settling on normal physiological wrinkling.
- **Hyperhidrosis.** Rapid wrinkling of the hands with a burning sensation has been reported in a patient concomitantly with palmar hyperhidrosis after exposure to water.[2] That patient was administered a topical 15% aluminium chloride hexahydrate solution every other day and was then able to be immersed in water for up to 30 minutes without symptoms. In the case presented above, the patient and her parents did not report any excessive sweating on her palms or other areas of her body.
- **Drug-induced AWP.** Some medications have been reported to induce wrinkling of the palms on exposure to water, especially COX inhibitors, such as aspirin,[3,4] indomethacin[5] and rofecoxib.[6] The effect ceases after discontinuation of the drug. This patient had not been given any medications in the three months before review.
- **AWP secondary to cystic fibrosis (CF) carriage.** This is the correct diagnosis. AWP is characterised by the transient development of oedematous whitish plaques on the palms, namely the 'hand-in-the-bucket' sign, on exposure to water. It was first reported and is still primarily reported in patients with CF and in CF carriers.[7,8] A case-control study showed that the average time to wrinkling was less in CF

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carriers compared with controls, and even less in patients with CF.[1] More recently, it was reported that the specific ΔF508 mutation within the *CFTR* gene predisposes patients to AWP.[9] To help understanding of the genotype-phenotype correlations, a case-control study was performed and showed that patients who were homozygous for the ΔF508 mutation had the highest wrinkling scores compared with CF patients with heterozygous or other mutations.[10] The molecular mechanism by which CF causes AWP is incompletely understood; however, it is thought to be related to the excessive intracellular water absorption and retention that is caused by the malfunctioning chloride channel that the mutated *CFTR* gene encodes. In Australia, one in 25 Caucasian people is a carrier of the CF gene.

## Diagnosis and investigations

The diagnosis of AWP is based on a clinical history and physical examination. Genetic testing for CF carriage is recommended for future genetic counselling.

## Management

There is currently no targeted therapy for AWP. However, some patients have reported relief with antiperspirants such as daily 20% aluminium chloride hexahydrate, bathing the affected area (typically just the hands) in salt water and supportive therapies such as antihistamines to reduce itch (not a common feature). Botulinum type A toxin injections have been reported to be successful, even in patients without known hyperhidrosis.[11] It is important to be aware of this skin sign because it is a diagnostic clue that a patient may be a CF carrier or have atypical CF, which has important clinical consequences for the patient and their future progeny.[12]

## Future progress

With the advent and approval of small molecules such as ivacaftor, lumacaftor and tezacaftor that directly target the malfunctioning chloride channel that the *CFTR* gene encodes, it may be possible that in future topical formulations of these drugs may be applied to patients with AWP. MT

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COMPETING INTERESTS: None.

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