

# Cystic Fibrosis Research News

## Title:

A false positive newborn screening result due to a complex allele carrying two frequent CF-causing variants.

## Authors:

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## What was your research question?

Numerous countries have recently implemented mandatory newborn screening (NBS) programs for cystic fibrosis (CF), reducing delays in diagnosis, facilitating a more proactive approach to disease management. This study reviews the unforeseen case of two frequent CF-causing variants carried on the same chromosome, found in an infant who was screened positive.

## Why is this important?

After the identification of one or two CFTR mutations in a newborn, a familial segregation study is critical to confirm that the patient inherited each mutation from a parent, confirming the diagnosis of cystic fibrosis. Family genetic studies are particularly useful in newborns not displaying clinical signs of the disease.

## What did you do?

A newborn who was positive for CF on NBS was found to have the CF-causing mutations p.Phe508del (F508del) and c.3140-26A>G (3272-26A>G). After the first medical consultation at the CF center, it was recommended that we investigate genetic samples from the parents to assess their contribution to the two mutations. In a second step, we performed a more in depth study of the family genetics through three generations including the child, her parents and the maternal grand-parents.

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## What did you find?

The two variants p.Phe508del (F508del) and c.3140-26A>G (3272-26A>G) were both carried by the mother of the newborn, whereas the father did not carry a CF-causing mutation. This result was confirmed by the analysis of the maternal grand-parents. Then, the baby and her mother underwent a thorough clinical examination, which failed to reveal any clinical symptoms of CF.

## What does this mean and reasons for caution?

This study of the family genetics finally ruled out the diagnosis of CF, which was initially suggested despite three inconclusive Sweat Chloride Tests. This case highlights the need of precautions in the announcement of CF diagnosis, considering the anxiety induced and the resulting constraints in daily life.

## What's next?

This finding provides new arguments that before a final diagnosis of CF is announced to families, clinicians should have both valid Sweat Chloride Test results and/or a complete assessment of the family genetics.

## Original manuscript citation in PubMed

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