

FAMILIAL MEDITERRANEAN FEVER

GENETIC TESTING



What is familial Mediterranean fever?

Familial Mediterranean fever (FMF) is an inherited autoinflammatory disease characterized by episodes of recurrent fever and pain in the abdomen, chest, and joints. Symptoms are attributed to decreased levels of a protein called pyrin (also known as marenstrin), which is involved in the body's immune response by helping to regulate inflammation. FMF is also known as familial paroxysmal polyserositis.^{1,2}

What are the symptoms of familial Mediterranean fever and what treatment is available?

FMF is a disease with a range of clinical symptoms and variable age of onset. Symptoms of FMF usually begin in childhood or adolescence in approximately 80% of FMF patients.³ Severity of disease may vary, even within families.¹ There are two types of FMF:

- FMF type 1 includes¹:
 - Recurrent episodes (typically lasting 24-48 hours) of fever with or without skin rashes
 - Recurrent episodes (typically lasting 24-48 hours) of painful inflammation of the chest, abdomen, and joints
 - Amyloidosis (a buildup of protein deposits in the body's organs and tissues) leading to life-threatening kidney failure in severe cases
- FMF type 2 includes¹:
 - Amyloidosis as the first clinical manifestation of disease in an otherwise asymptomatic individual

Currently, there is no known cure for FMF. However, a medication called colchicine has been successful in preventing attacks for individuals with specific genetic mutations. It also may prevent amyloidosis, even in those

unresponsive to the drug for attacks. For individuals with kidney failure due to amyloidosis, kidney transplantation may be needed. With early and regular treatment, most individuals with FMF are able to live a normal life span.¹

How is familial Mediterranean fever inherited?

FMF is an autosomal recessive disease caused by mutations in the *MEFV* gene.¹ An individual who inherits one copy of an *MEFV* gene mutation is a "carrier" and is typically not expected to have related health problems. A subset of individuals with only one identified copy of a gene mutation may have symptoms, but the cause of symptoms remains unclear.¹ An individual who inherits two mutations in this gene, one from each parent, is expected to be affected with FMF. As clinically indicated, testing of family members may be considered to confirm the inheritance of one mutation from each parent.

If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy. Therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Carrier Frequency in Select Ethnic Groups

Ethnicity	Carrier Frequency
Turkish ⁴	~1 in 5
Arabic ³	~1 in 5
Armenian ⁵	~1 in 5
North African Jewish ⁶	~1 in 7
Ashkenazi Jewish ⁷	~1 in 81*

* The carrier frequency in healthy Ashkenazi Jewish individuals has been reported to be as high as 1/5.¹ However, based on the observed incidence of disease, the carrier frequency corresponds to 1 in 81.⁷

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Who is at risk for familial Mediterranean fever?

FMF can occur in individuals of all races and ethnicities, but is most common in individuals of Mediterranean descent, particularly those of Arabic, Armenian, Turkish, North African Jewish, and Ashkenazi Jewish ancestry.³

Having a relative who is a carrier or is affected can also increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

- National Library of Medicine
<http://ghr.nlm.nih.gov/condition/familial-mediterranean-fever>
- National Human Genome Research Institute
www.genome.gov/12510679
- Emedicine
www.emedicine.medscape.com/article/330284-overview
- Chicago Center for Jewish Genetic Disorders
www.jewishgenetics.org/?q=content/familial-mediterranean-fever
- Mayo Clinic
www.mayoclinic.com/health/familial-mediterranean-fever/DS00766

Note: This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

References

1. Shohat M, Halpern GJ. Familial Mediterranean fever. GeneReviews. Available at <http://www.ncbi.nlm.nih.gov/books/NBK1227>. Accessed: Jan 27, 2012.
2. McKusick VA, O'Neill M. Familial Mediterranean fever. OMIM. Available at <http://omim.org/entry/249100>. Accessed: Jan 29, 2012.
3. El-Shanti H, Majeed H, El-Khateeb M. Familial Mediterranean fever in Arabs. *The LANCET*. 2006; 367: 1016-1024
4. Turkish FMF Study Group. Familial Mediterranean fever (FMF) in Turkey. *Medicine*. 2005; 84:1-11.
5. Sarkisian T, Ajrapetyan H, Shamsuvaryan G. Molecular study of FMF patients in Armenia. *Current Drug Targets – Inflammation & Allergy*. 2005; 4: 113-116
6. Gershoni-Baruch R, Shinawi M, Leah K, Badarnah K, Brik R. Familial Mediterranean fever: prevalence, penetrance and genetic drift. *European Journal of Human Genetics*. 2001; 9: 634-637.
7. Lidar et al. Familial Mediterranean fever in Ashkenazi Jews: The Mild End of the Clinical Spectrum. *J Rheumatol*. 2010; 37:422-425.



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