

Familial Mediterranean fever

This is the lay version of the EULAR recommendations for people with familial Mediterranean fever. The original publication can be downloaded from the EULAR website: www.eular.org.

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Introduction

Recommendations give advice to doctors and patients about the best way to treat and manage diseases. EULAR has written recommendations on the management of people with familial Mediterranean fever.

The recommendations were written by doctors, nurses and patients. They looked at the evidence on the management of people with familial Mediterranean fever. They also discussed their expert opinion to achieve a level of agreement.

What do we already know?

Familial Mediterranean fever (often shortened to FMF) is an inherited (or genetic) autoinflammatory disease. Autoinflammatory diseases are a group of conditions where a person's immune system attacks its own body tissues, causing inflammation. FMF is common in people who have ancestors from the Mediterranean region. It causes painful inflammation in the joints, lungs and abdomen. People with FMF get recurrent fevers and aches. FMF is often diagnosed during childhood with a careful history and examination, as well as blood and genetic tests.

What do the recommendations say?

Overall, there are 18 statements or recommendations. Each recommendation is based on available scientific evidence or expert opinion. The more stars a recommendation has the stronger the evidence is and the more important it is that you and your doctor follow it.

One star (*) means it has limited evidence.

Two stars (**) means it has some evidence.

Three stars (***) means it has quite a lot of evidence.

Four stars (****) means it is supported by a lot of evidence.

- **A doctor with experience of the disease should diagnose and initially treat.***
 FMF can be diagnosed by physicians with different specialties, such as paediatric and adult rheumatologists, internists, clinical geneticists, nephrologists and gastroenterologists. Once you have been diagnosed and you have been given a treatment, your general practitioner or paediatrician can look after you, with annual visits to the specialist.
- **The goal of treatment is to control attacks and minimize inflammation in between attacks.****
 Controlling and reducing the number of attacks of FMF will improve your general quality of life. Completely stopping the attacks may not be possible if your disease is very severe. Minimising the inflammation in your body helps to prevent long-term complications such as amyloidosis, where a protein called serum amyloid A builds up in the body's tissues. People with amyloidosis might have kidney problems or be at risk of dying early.
- **Treatment with colchicine should start as soon as a diagnosis is made.******
 Colchicine is an anti-inflammatory drug derived from a plant extract. It can prevent attacks of FMF. It is taken as a pill, usually at a starting dose of 0.5 mg per day, but this will depend on your age and your disease severity.
- **The dose of colchicine can be split to help prevent side effects.***
 Colchicine can cause stomach upsets and diarrhea. These side effects can be reduced by splitting the dose and taking half in the morning and half in the evening. This can help to reduce side effects, and might mean that people are less likely to skip doses.
- **If FMF attacks or inflammation continue then the colchicine dose can be increased.****
 Your doctor may increase your colchicine up to a daily dose of 2 mg in children and 3 mg in adults, or as much as you can tolerate before feeling unwell. It is important that you do not change your dose yourself without talking to your doctor first.
- **Alternative biologic treatments can be considered in people who have taken the maximum dose of colchicine properly without skipping doses, but have not seen an improvement in their FMF.*****
 Sometimes people might be resistant or non-responsive to colchicine. If this happens to you, your doctor may suggest that you try adding a biologic drug that blocks the inflammation. There is some evidence that biologic drugs that target interleukin 1 may be effective in FMF resistant to colchicine.
- **Treatment should be intensified in people with amyloidosis using the maximum tolerated dose of colchicine plus biologics if required****
 Amyloidosis is a complication of FMF where the body makes a protein called serum amyloid A, which then builds up in the tissues and organs. People with this might have kidney problems or be at risk of dying early. If you have amyloidosis you will need higher doses of colchicine, and may also need to take a biologic drug.
- **You should be monitored every 6 months***
 You should see your doctor once every 6 months to make sure that you are taking your medicine properly, that it is working for you, and that you do not have side effects. This monitoring might be more often than every 6 months when you are first diagnosed, or in children or people with complications. You might be given a diary to record your symptoms and temperature regularly. It is very important not to skip doses of colchicine because this can affect how well it prevents attacks.
- **If you are taking colchicine, your liver enzymes should be monitored regularly. If they are raised you may need to reduce your dose.***

Liver enzymes are monitored with blood tests. If your liver enzymes are higher than two-times the upper limit of normal, your colchicine dose should be reduced. Your doctor may do more investigations to see what has caused the change.

- **If you have decreased renal (kidney) function, the risk of toxicity is very high.****
If renal function is impaired there may be an increased risk of colchicine toxicity. Thus your dose should be reduced to protect your kidneys from damage.
- **Colchicine toxicity is a serious complication and steps should be taken to prevent it.****
You should not take more than the maximum dose of 3 mg daily in adults and 2 mg daily in children. Some other drugs can affect the way that the body deals with colchicine. You should let your doctor know that you are taking colchicine if you are prescribed macrolides, ketoconazole, ritonavir, verapamil, ciclosporin, or statins.
- **FMF attacks can be confused with other possible causes. During attacks you should continue your normal dose of colchicine and use an NSAID.****
Symptoms of FMF can be confused with other illnesses. If you or your doctor are not sure you should monitor your symptoms carefully in case you are unwell with something else. During attacks you can take a non-steroidal anti-inflammatory drug (often shortened to NSAID) to reduce pain.
- **Do not stop taking colchicine if you are pregnant or planning to become pregnant, or while you are breastfeeding.****
Colchicine is not known to be dangerous to your baby if you are pregnant or trying to conceive, or if you are breastfeeding. If you stop taking your medicine you could have more FMF attacks, which could increase your chances of a miscarriage. If you are pregnant, there is no evidence at the moment to support having an amniocentesis test to check on the baby.
- **Men do not normally need to stop taking colchicine before trying to get their partner pregnant.****
Routine doses of Colchicine is not thought to affect a man's fertility, or to pose any risk to a baby conceived while its father was taking the drug. Very rarely a man might have semen that contains no sperm (azoospermia) or low numbers of sperm (oligospermia) caused by colchicine. In this case, the drug can be temporarily reduced or stopped to allow conception.
- **If you have chronic arthritis you might need additional medicines, such as DMARDs, steroid injections or biologics.****
If you have chronic arthritis as well as FMF, you might need to take more medicines to treat it. Normal treatments for inflammatory arthritis are disease modifying anti-rheumatic drugs (shortened to DMARDs), steroid injections into the affected joints, or biologic drugs that prevent inflammation. For sacroileitis accompanying FMF; anti TNF drugs may be considered.
- **Steroids can relieve symptoms of prolonged fever and muscle pain.****
If you have fever and muscle pain that lasts for more than 5 days, you can take glucocorticoids (steroid medicines) to relieve the symptoms. NSAIDs and biologics that block a molecule called interleukin-1 (IL-1) might also work.
- **If you have been stable with no attacks for more than 5 years, dose reduction could be considered.***
If your FMF is stable and the results of your blood tests show you have no inflammation, you may be able to reduce your dose of colchicine. You can only reduce your dose after consulting your doctor, ,

and only if you have continued monitoring to make sure you are well. This is possible only in a few patients.

Summary

Overall, the recommendations say that it is important for you and your doctor to work together to monitor and manage your disease and particular symptoms, and to get the best possible results from treatment. If you have FMF these recommendations will give you suggestions or ideas about what should be discussed with your doctor.

If you have any questions or concerns about your disease or your medication, speak to your doctor.