

Warfarin resistance

Description

Warfarin resistance is a condition in which individuals have a high tolerance for the drug warfarin. Warfarin is an anticoagulant, which means that it thins the blood, preventing blood clots from forming. Warfarin is often prescribed to prevent blood clots in people with heart valve disease who have replacement heart valves, people with an irregular heart beat (atrial fibrillation), or those with a history of heart attack, stroke, or a prior blood clot in the deep veins of the arms or legs (deep vein thrombosis).

There are two types of warfarin resistance: incomplete and complete. Those with incomplete warfarin resistance can achieve the benefits of warfarin treatment with a high dose of warfarin. Individuals with complete warfarin resistance do not respond to warfarin treatment, no matter how high the dose. If people with warfarin resistance require anticoagulant therapy and take the average warfarin dose, they will remain at risk of developing a potentially harmful blood clot.

Both types of warfarin resistance are related to how the body processes warfarin. In some people with warfarin resistance, their blood-clotting process does not react effectively to the drug. Others rapidly break down (metabolize) warfarin, so the medication is quickly processed by their bodies; these individuals are classified as "fast metabolizers" or "rapid metabolizers" of warfarin. The severity of these abnormal processes determines whether the warfarin resistance is complete or incomplete.

Warfarin resistance does not appear to cause any health problems other than those associated with warfarin drug treatment.

Frequency

Warfarin resistance is thought to be a rare condition, although its prevalence is unknown.

Causes

Many genes are involved in the metabolism of warfarin and in determining the drug's effects in the body. Certain common changes (polymorphisms) in the *VKORC1* gene account for 20 percent of the variation in warfarin metabolism due to genetic factors. Polymorphisms in other genes, some of which have not been identified, have a smaller effect on warfarin metabolism. The polymorphisms associated with warfarin resistance

often differ by population and ethnic background.

The *VKORC1* gene provides instructions for making a vitamin K epoxide reductase enzyme. The *VKORC1* enzyme helps turn on (activate) clotting proteins in the pathway that forms blood clots. Warfarin prevents (inhibits) the action of the *VKORC1* enzyme by binding to the enzyme and preventing it from binding to and activating the clotting proteins, stopping clot formation. Certain *VKORC1* gene polymorphisms lead to the formation of a *VKORC1* enzyme with a decreased ability to bind to warfarin. This reduction in warfarin binding causes incomplete warfarin resistance and results in a higher dose of warfarin needed to inhibit the *VKORC1* enzyme and stop the clotting process. If the *VKORC1* enzyme cannot bind to any warfarin, the result is complete warfarin resistance.

While changes in specific genes affect how the body reacts to warfarin, many other factors, including sex, age, weight, diet, and other medications, also play a role in the body's interaction with this drug.

[Learn more about the genes associated with Warfarin resistance](#)

- UGT1A1
- VKORC1

Additional Information from NCBI Gene:

- ABCB1
- CALU
- CYP2A6
- CYP4F2
- NQO1

Inheritance

The polymorphisms associated with this condition are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to result in warfarin resistance. However, different polymorphisms affect the activity of warfarin to varying degrees. Additionally, people who have more than one polymorphism in a gene or polymorphisms in multiple genes associated with warfarin resistance have a higher tolerance for the drug's effect or are able to process the drug more quickly.

Other Names for This Condition

- Coumarin resistance
- Poor metabolism of coumarin

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Warfarin response (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0750384/>)

Genetic and Rare Diseases Information Center

- Warfarin resistance (<https://rarediseases.info.nih.gov/diseases/12721/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Catalog of Genes and Diseases from OMIM

- COUMARIN RESISTANCE (<https://omim.org/entry/122700>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28warfarin+resistance%5BTIAB%5D%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

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