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Genetics Education Canada: Knowledge Organization
Centre d'éducation en génétique canadien: Connaissances organisées
on the run

INHERITED THROMBOPHILIA

FACTOR V LEIDEN

FVL is a very common inherited thrombophilia associated with a moderate increased lifetime risk for venous thromboembolism (VTE). Genetic testing for carrier status of can be controversial and is only indicated in a few circumstances where changes to clinical management would be affected. Genetic testing is not recommended the general population nor for the indication of early pregnancy loss. Treatment of VTE in FVL carriers should follow standard guidelines.

Abbreviations Factor V Leiden - FVL; Venous thromboembolism - VTE; Activated protein C - APC

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What is factor V Leiden?

FVL is an inherited clotting disorder, thrombophilia. It is characterized by a poor anticoagulation response to activated protein C (APC). Individuals with this type of APC resistance have a variant (called the Leiden variant) in the FV gene resulting in the production of a FV protein that is very slowly inactivated and so more thrombin is generated. For more on the coagulation pathway visit Calgary Guide to Understanding Disease [Accessed Nov 2022]

THE CALGARY GUIDE TO UNDERSTANDING DISEASE

How common is FVL?

FVL is the most common inherited thrombophilia.

FVL carrier status (heterozygous, one copy of FVL) is observed in 20% of an unselected, symptomatic with VTE population. When there is also a strong family history of VTE, FVL is observed in 40% of individuals.

In the general (asymptomatic) population, frequency depends upon ethnicity.

- 3-7% of individuals of European, Mediterranean, and Middle Eastern ancestry are carriers of FVL
- It is extremely rare for individuals of Asian, African or, Indigenous Australian ancestry to carry a FVL variant

Generalizing to the Canadian population, over one million Canadians are carriers of the FVL variant.

It is rare for an individual to carry two copies of the FVL variant (homozygous).
The prevalence is estimated to be about 1 in 5,000.

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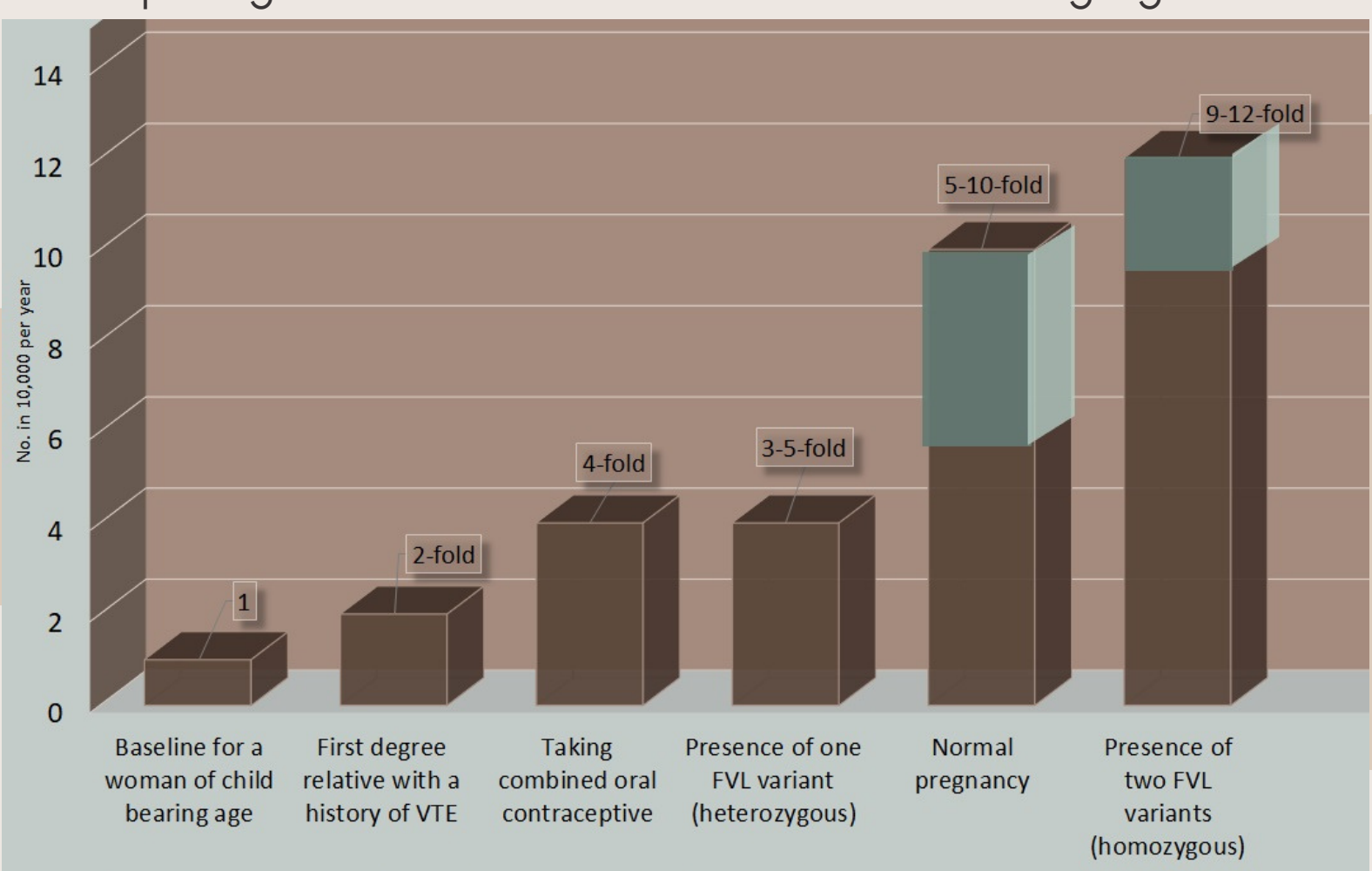
What are the associated risks?

General risk factors for a VTE are age, surgery, cancer, pregnancy, recent heart attack, prolonged immobilization (e.g. long air travel), and genetic factors.

Carrying the FVL variant is associated with an increased lifetime risk for VTE, but the absolute risk is very small and most individuals with FVL never experience a clot.

Those with one FVL variant (heterozygous) have a 3-5 fold increased lifetime risk of VTE. See figure below as an example comparing risk states for a female of child bearing age.



Comparison of risk for venous thromboembokism (VTE) in a female of child bearing age between risk factors, where baseline risk is 1 in 10,000 per year

Following a first unprovoked VTE, FVL carrier status is not associated with increased recurrence risk. Clinical circumstances of the event, adequacy of early treatment, and individual risk factors determine recurrence risk.

FVL carrier status is not associated with increased risk of mortality.

When should genetic testing NOT be considered?

Genetic testing for FVL carrier status can be controversial and general population screening **is not recommended.**

There are predicted harms to carrier testing in asymptomatic individuals such as unnecessary exposure to thromboprophylaxis, or modifications to plans for birth control, surgery, travel and improperly labelling as an individual with a disease.

FVL carrier testing **is not recommended** for women following early pregnancy loss.

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When should genetic testing be considered?

FVL carrier testing may be considered in the following scenarios when the results of testing would affect clinical management:

- Persons with a first, unprovoked VTE who are planning to stop anticoagulation
- Females with a family history of VTE or a known inherited thrombophilia who are considering:
  - estrogen contraception or hormone replacement
  - prophylactic anticoagulation during pregnancy

How is VTE managed in FVL carriers?

VTE management depends on the clinical circumstances.

The first acute thrombosis should be treated according to standard guidelines. (see CHEST, Thrombosis Canada). There is no evidence to support improved health outcomes or changes to clinical management would be guided by FVL testing.

FVL carrier status alone is not an indication for long term anticoagulation therapy. The decision should be made based on an assessment of the risks for VTE recurrence and anticoagulant-related bleeding.

What should carriers of the FVL know?

Carriers should be informed about:

- Circumstances that might increase the likelihood of VTE (obesity, age, surgery, reduced mobility due to injury or travel, use of oral contraceptives, HRT, or SERMs, and pregnancy)

- The signs and symptoms of VTE that require immediate medical attention
- The potential need for prophylactic anticoagulation in high-risk circumstances

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