Thrombophilia

- Thrombophilia may be defined as the tendency to develop thrombosis:
  - Hereditary thrombophilia (congenital or juvenile), is a genetically determined tendency to develop venous thrombosis.
  - Acquired thrombophilia.

Classification

- **Hereditary thrombophilia (congenital)**
  - Associated with a family history of venous thrombosis (in most cases).
  - Recurrent thrombosis in certain patients.
  - Not always associated with a clear triggering factor.
  - Affects young subjects: < 60 years.

- **Acquired thrombophilia**
  - No associated family history (generally).
  - Associated with transient triggering event such as:
    - Traumatic injury.
    - Pregnancy - in particular during the post-partum period.
    - Immobilisation (i.e., stasis, long flights, etc).
    - Post-operative period.
    - Advanced age (first event > 60 years).
  - Oestrogen therapy.
  - Antiphospholipid antibodies.
  - Can also be associated with other clinical disorders such as:
    - Cancer.
    - Heparin-induced thrombocytopenia.

Diagnostic tests for thrombophilia

- **Prelimary Screen:**
  - Antithrombin, Protein C, Protein S, resistance to activated Protein C / Factor V Leiden, prothrombin gene mutation, lupus anticoagulants (LA) and antiphospholipid antibodies (APA).

- **Secondary Screen:**
  - Fibrinogen, homocysteine.
  - Investigation of fibrinolysis (tPA, etc.)
  - Assay of factor VIII, etc.

Prevalence in thrombotic subjects

CAUSES	USUAL VALUES	RELATIVE RISK	PREVALENCE
Antithrombin	80 - 120%	10-20 in heterozygous patients	1-2% in patients with VTE
Protein C	70 - 130%	6	3% in patients with VTE
Protein S*	60 - 140%	5 in patients	0.05-1% in the general population 2-3% in thrombotic subjects
FV leiden	———	3-5 heterozygous	5% in the general patients population >20% in thrombotic subjects
FII genous polymorphism	———	2-3 heterogenous patients	2% in the European population
αβ2Gp1 + ACL	———	2.2	———

*depends on age and sex

- **Other tests**
  - Other Haemostasis elements.
- **Sample collection procedure**

Samples used for confirmation of thrombophilia must be collected at least 3 months after the latest thrombotic event and in accordance with the time limits associated with the test to be performed after the end of treatment.

- Samples should not be taken in the following cases:
  - During acute episodes of DVT/PE
  - During oral anticoagulant treatment with vitamin K antagonists, PC and PS levels are reduced by 50% and levels of activity are reduced.
  - It is necessary to wait one month after discontinuation of treatment with vitamin K antagonists before performing Protein C and Protein S assays.
  - In the case of heparin treatment, which could reduce antithrombin levels
  - In pregnant women and for up to 3 months after childbirth
  - In patients on oestrogen therapy until 2 cycles after treatment discontinuation (e.g. contraceptive pills)
  - In patients treated with L-asparaginase
  - In patients with nephritic syndrome, hepatic impairment, DIC or an inflammatory condition.
  - In the case of positive screening tests for LA, further screening should be repeated after 12 weeks.

Low levels of PC and PS are seen in normal paediatric samples.
In tests performed on paediatric samples, normal values for patients of the same age group should be established before the diagnosis is established.

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