FACTOR V DEFICIENCY

TERM DEFINITION

Factor V (FV) deficiency is a rare bleeding disorder, which may be congenital (homozygous or compound heterozygous mutation) or acquired.

TYPES

CONGENITAL

Congenital FV deficiency affects an estimated 1 in 1,000,000 individuals and represents 9% of rare bleeding disorders diagnoses.

ACQUIRED

Acquired FV deficiency, incidence estimated at <0.5 per million person years, usually occurs after the sixth decade of life.

CAUSES

CONGENITAL

- Missense, nonsense, splicing, and insertion / deletion mutations of the FV gene.

ACQUIRED

Inhibitors

- Idiopathic
- Drugs
- Exposure to bovine thrombin
- Malignancy
- Infection
- Autoimmune disease

Deficiency

- Amyloidosis

FACTOIDS

There is a poor correlation between FV levels and severity of bleeding.

Inhibitor may be clearance-enhancing, not neutralizing, leading to normal mixing study.

Platelets contain 20% of blood FV.

DIAGNOSIS

CONSIDER

Consider the diagnosis in a patient with:

Congenital deficiency:

- Bleeding early in life
- Elevated PT *and* aPTT

Acquired deficiency:

- Recent onset of bleeding symptoms, especially in older adults
- Lack of previous bleeding symptoms, especially in association with previous hemostatic challenges
- No family history of congenital / inherited deficiency of FV (or other coagulation factor deficiencies)
- Elevated PT and aPTT

CONFIRM

Confirm the diagnosis in a patient with:

Congenital deficiency:

- Reduced FV activity determined by specific factor assay
- Correction of prolonged PT and aPTT by normal plasma (mixing study)

Acquired deficiency:

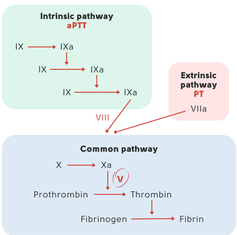
- Reduced FV activity determined by specific factor assay
- Mixing study
  - Correction of prolonged PT and aPTT by normal plasma if there is amyloid-associated deficiency of FV or clearance-enhancing antibody
  - No correction if there is a neutralizing antibody against FV

PT, prothrombin time; aPTT, activated partial thromboplastic time; FV, factor V

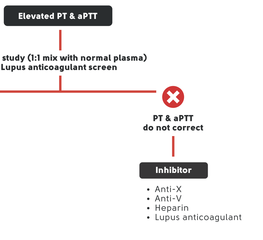
DIFFERENTIAL DIAGNOSIS OF INCREASED PT & aPTT

Factor V (FV) is a rare cause of elevated PT and aPTT. There are several ways to increase both the PT and the aPTT:

- Deficiency of, or inhibitor against, a factor(s) in the **common pathway** (namely, FV and FX)
- Deficiency of, or inhibitor against factors in both the **extrinsic and intrinsic pathways:**
  - Heparin (though primarily affects the aPTT)
  - Warfarin (though primarily affects the PT)
  - Liver disease
  - Disseminated intravascular coagulation
  - Lupus anticoagulant (primarily affects the aPTT)

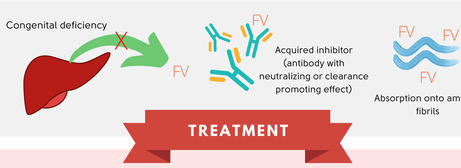


Shown to the right is a clotting cascade illustrating intrinsic, extrinsic, and common pathways. FV (V, circled) is a co-factor that accelerates FX-mediated cleavage of prothrombin in the common pathway. The aPTT monitors the intrinsic pathway, PT the extrinsic pathway.



*In patients with FV inhibitor, the mixing study may be negative because the antibody increases clearance of FV, rather than inhibit its function.

PROXIMATE MECHANISMS



TREATMENT

HEMOSTATIC TREATMENT

- There is no FV concentrate
- Severe bleeding is treated with:
  - Fresh frozen plasma (1% activity/ml)
  - Platelet transfusions (platelets contain FV)
  - Fibrinolytic agents

ERADICATION OF INHIBITOR

- Applies if an inhibitor is present
- High dose corticosteroids with or without one of the following:
  - Cyclophosphamide
  - Rituximab

HISTORY OF MEDICINE

Factor V (FV) deficiency was first described in a Norwegian patient in 1943 and reported by Dr. Paul Owren in 1947. It was known for some time as **Owren's disease.**

FV inhibitors were first described in the 1950s in patients exposed to bovine thrombin during surgery or following transfusion of fresh frozen plasma in patients with severe congenital FV deficiency.

NOTES

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The Blood Project
ENCYCLOPEDIA OF BLOOD