The development of FVIII inhibitors in hemophilia A patients results from the inability of the immune system to mount a counteractive tolerogenic response.

Severe hemophilia A

Insufficient levels of pro-coagulant factor VIII (FVIII) → Bleeding disorder

Intravenous administration of therapeutic FVIII → Development of inhibitory anti-factor VIII antibodies (inhibitors)

Treatment

- Repercussions on the clinical management of the patients
- Reduction of the quality of life

- All hemophilia A patients treated with FVIII develop an immune response to therapeutic FVIII
- The onset of neutralizing antibodies to FVIII results from an [inability to develop a counteractive antigen-specific tolerogenic response](#), rather than from an exacerbated activation of the immune system at the time of FVIII administration

5-30% of the patients fail to develop active immune tolerance to FVIII

Varthaman and Lacroix-Desmazes *et al.*, Haematologica, 2019