

Indicators for Immune Testing



- ✦ The indications are as follows:
- ✦ (a) two IVF failures after age 35 or 3 IVF failure before age 35,
- ✦ (b) poor egg production from a stimulated cycle (less than 6 eggs),
- ✦ (c) blighted eggs,
- ✦ (d) idiopathic (unknown cause) infertility,
- ✦ (e) previous immune problems (ANA positive, rheumatoid arthritis, and/or lupus),

Laboratory Studies

- ✦ Antiphospholipid Antibodies Panel (18 antibodies)
- ✦ Antinuclear Antibodies Panel (6 antibodies)
- ✦ Antithyroid Antibodies Panel (2 antibodies)
- ✦ Antipaternal Leukocyte Antibodies Panel (2 antibodies)
- ✦ Immunophenotype (7 parameters)
- ✦ Natural Killer Cell Activation Assay
- ✦ Natural Killer Cell with IVIg Assay (12 parameters)
- ✦ Human Leukocyte Antigens (HLA) ABC
- ✦ Human Leukocyte Antigens (HLA) DR/DQ
- ✦ DQ α (Genotyping)
- ✦ DQ β (Genotyping)

Antiphospholipid Antibodies Panel



- ✦ Anticardiolipin antibodies -- IgG, IgM, IgA
- ✦ Antiphosphoglycerol antibodies -- IgG, IgM, IgA
- ✦ Antiphosphoserine antibodies -- IgG, IgM, IgA
- ✦ Antiphosphoethanolamine antibodies -- IgG, IgM, IgA
- ✦ Antiphosphatidic acid antibodies -- IgG, IgM, IgA
- ✦ Antiphosphoinositol antibodies -- IgG, IgM, IgA
- ✦ Lupus anticoagulant (LA)
- ✦ VDRL

Anti B2 glycoprotein

- ✦ B2 glycoprotein is a multifunctional plasma protein that can bind cardiolipin. While binding structure of both of them change.
- ✦ B2 glycoprotein has a complex involvement in agglutination. It alters aggregation of platelets by inhibiting serotonin release by platelets.

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- ✦ Normally B2 glycoprotein has anticoagulation activity in serum by inhibiting coagulation factors.
 - ✦ B2 glycoprotein bind to negatively charged agglutinating and inhibits activation of intrinsic blood coagulation pathway.
 - ✦ B2 glycoprotein causes a reduction of prothrombinase binding site on platlatets.
 - ✦ B2 glycoprotein inhibits generation of factor Xa and activation of factor XIIa.



✦ Anti B2 glycoprotein are found in both in some infectious and autoimmune diseases.

Antinuclear Antibody Panel



- ✦ ANA Titer
- ✦ Double stranded DNA
- ✦ SSA
- ✦ SSB
- ✦ RNP
- ✦ SM

- ✦ Antihistone Antibody

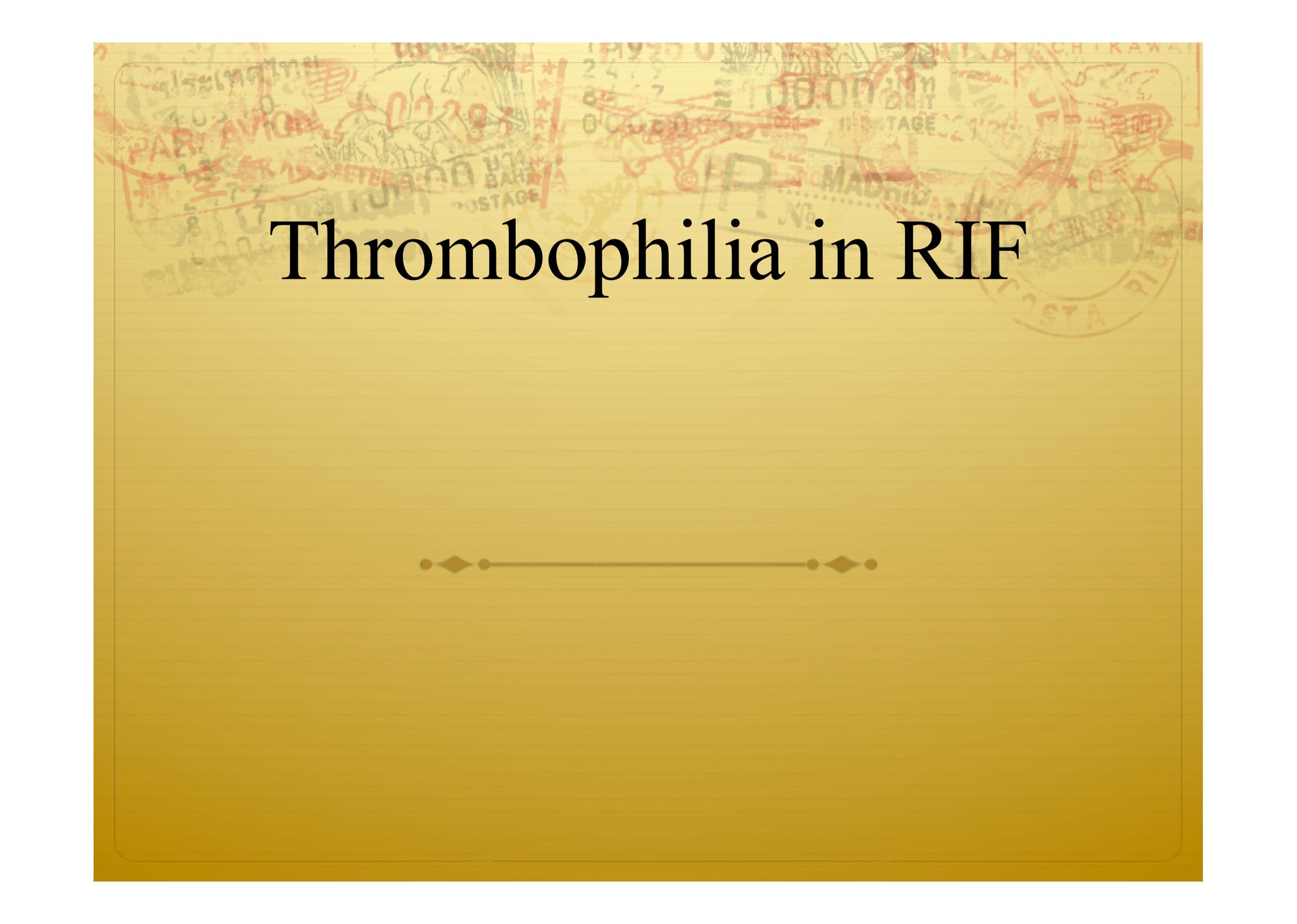
Antithyroid Antibodies Panel



- ✦ Anti-TPO
- ✦ Anti-thyroglobulin
- ✦ Anti-TSHR
- ✦ Tissue transglutaminase

Immunophenotype

- ✦ Natural Killer Cells (CD16+CD56+)
- ✦ B1-Cells (CD5+CD19+)



Thrombophilia in RIF



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- ✦ Heparan sulphate proteoglycans (HSPGs) are expressed throughout the reproductive tract and are involved in the regulation of endometrial cycling.
 - ✦ The primary biological activity of heparin is anticoagulation or the antithrombin effect, where heparin catalyzes the inhibition of factor Xa and thrombin.

Heparin

- modulates:
 - endometrial receptivity
 - decidualization of endometrial stromal cells and improves implantation.

- Increases:
 - production of prolactin
 - insulin-like growth factor (IGF-1)

- Inhibits:
 - production of insulin-like growth-factor-binding protein (IGFBP-1).

- These proteins plays an important role in endometrial development and receptivity during the ‘implantation window’.

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- ✦ heparin regulates heparin-binding epidermal growth factor (EGF), which is expressed maximally at the time of implantation, thus enhancing implantation, trophoblast invasion and promoting the early stages of embryo development.
 - ✦ It has been shown that LMWH can enhance invasiveness of extravillous trophoblast cells by inducing activity of specific metalloproteases (MMP).

Moreover,



- ✦ in the presence of APLS, apart from its antithrombin effect, LMWH prevents APA binding to the trophoblast cells
- ✦ Heparin has also been shown to block complement activation.
- ✦ modulates inflammatory responses in women with APA.

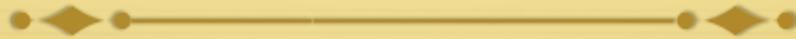


✦ In animal models:

heparin has been demonstrated to act on adhesion molecules like the E-cadherin system to regulate implantation.

✦ In *in vitro* models:

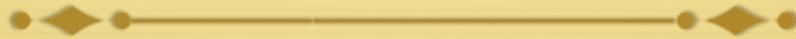
heparin has been shown to reduce aberrant apoptosis in the trophoblasts and enhance cell survival.



✦ So,

Heparin treatment can potentially enhance the implantation process.

Thrombophilia



✦ Major:

FVL, Prothrombin II, Antithrombin III or protein C or S deficiency, APL Syndrome

✦ Minor:

MTHFR, PAI-I