

# THE ANTIPHOSPHOLIPID SYNDROME

**NO PREDICTIVE TESTS**

**NO RX UNTIL THROMBOSIS**

**LIFETIME ANTICOAGULATION**

# Thrombotic Risk in Patients with APL

**Historical Risk: 61% LA 52% ACL 24% (-) (1)**

**Prospective Risk: 2%/year/SLE (2)  
3-7%/year/APL (3-5)**

1. Swadzba J et al: Pol Merkuriusz Lek 1:310-312, 1996
2. Hopkins Lupus Cohort
3. Finazzi G: Haematologica 82(1):101-105, 1997
4. Finazzi G et al: Am J Med 100(5):530-536, 1996
5. Cervera R et al: Medicine (Baltimore) 78(3):167-75, 1999

# Increased Risk of Thrombosis in APS

- **Increased Antibody Titer**
- **Multiple Reactivities**
- **Multiple Risk Factors**
  - atherosclerotic
  - genetic polymorphisms
  - predisposing historical events

# Protein Targets of Antiphospholipid Antibodies

Prothrombin



B2-glycoprotein I



Thrombomodulin

TF/TFPI



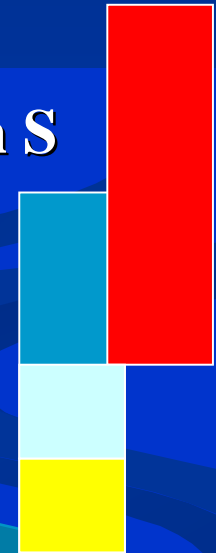
Annexin V



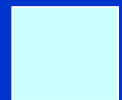
Protein C



C4BP B chain



Gla domain

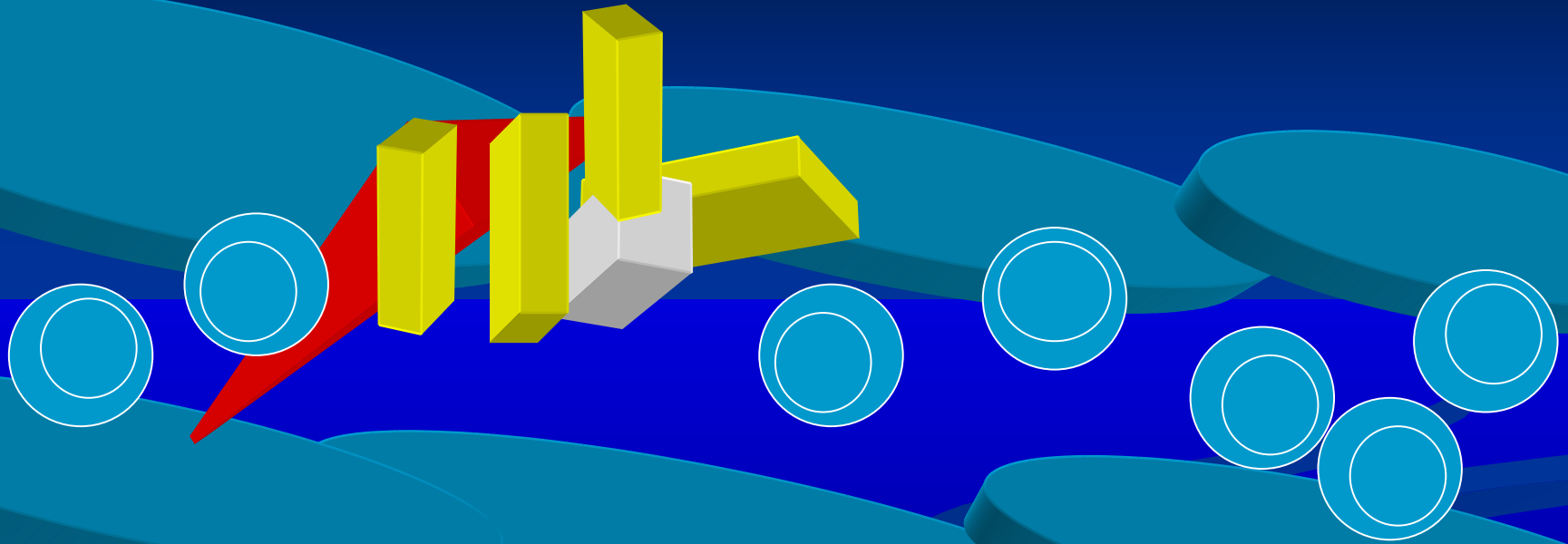


EGF-like domain



Complement Control Superfamily

# The Antiphospholipid Syndrome



**Apoptosis, inflammation, membrane changes**  
**Changes in conformation of anticoagulant proteins**  
**Antibody-mediated interference with these proteins**

# Conditions Associated with APL

**SLE (25%)**

**Thrombotic-related PPH (20%)**

**PPH (10%)**

**Cancer (19%)**

**alcoholism (11%)**

**age (7.1%)**

**atherosclerosis (6%)**

**leg ulcers (6%)**

# Probable Risk Factors

smoking

oral contraceptives

pregnancy

lipid/lipoprotein abnormalities

active inflammatory disease

any hypercoagulable factors

any atherosclerotic factors

# Probable Protective Factors

hydroxychloroquine

aspirin

ACE inhibitors

antioxidants

wine

genetic factors (epistasis)

# Clinical Diagnosis: Stroke

- Angiography:** Stenosis and subclinical occlusion
- Spect Scan:** Decreased bloodflow and perfusion: subclinical
- Echocardiogram:** High incidence (Lockshin)

# **Clinical Diagnosis: Renal**

**Thrombotic Renal Disease Resembling  
Class V (importance of biopsy)**

**Post renal-transplant thrombosis**

# Clinical Diagnosis: Pregnancy

Specificity of fetal death 76%

Specificity of first trimester loss 6%

80% of women with APS have fetal loss

**but**

50% of their losses are first trimester

villous infarction rare in first trimester loss

abn resistance of uterine arteries at 18-24 weeks

(velocimetry)

*Nayer R et al Hum. Pathol. 27:201-206, 1996.*

*Caruso A et al Obst Gynecol 82:970-977, 1993*

# TREATMENT FOR APLS

Close the Barn door after the horse has left

**Coumadin**

**Heparins**

**IVIG**

**New Antithrombotic Agents**

**(empiric use)**

# Therapeutic Range of Coumadin

**INR 2.0-3.0**

**Most Indications**

**INR 2.5-3.5**

**Mechanical Prosthetic Valves**

**Post-MI**

**APLS**



# PT/INR Response to Coumadin

## Endogenous Factors

Malabsorption

Edema

Hereditary or Acquired Resistance

Hyperlipemia

Hypothyroidism

Nephrotic Syndrome



# **PT/INR Response to Coumadin**

## **Exogenous Factors**

**Diet High in Vitamin K**

**Drug Interactions**

**Unreliable PT/INR**

**Patient Compliance**

**Medication Dosing Error**

# **Foods High in Vitamin K**

**Yes High in Vitamin K (lowers Coumadin effect)**

**Green, leafy vegetables**

**Apple Peel**

**Pistachios, or mixed nuts (not peanuts)**

**Vegetable oils**

**No Effect on Vitamin K**

**Beef, chicken, fish**

**Dairy**

**Grains**

**Stability of diet, not abstinence**