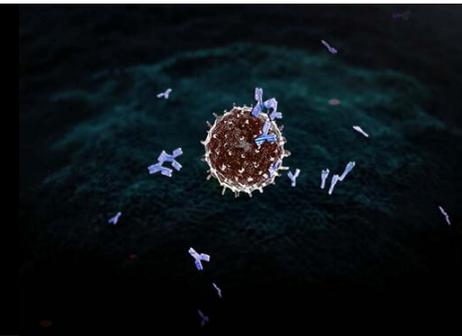


# Platelet Factor IV- Heparin Antibodies



Presenter: Michael J. Warhol, M.D.

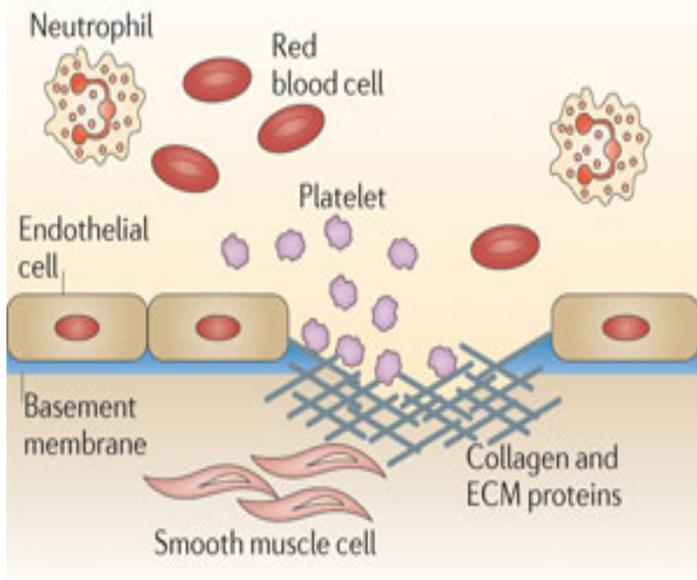
# Learning Objectives

- Describe the mechanism of interaction between Heparin and Platelet Factor 4
- Review the chemistry of Heparin
- Identify the consequences of antibodies to the Heparin Platelet Factor 4
- Examine the testing methodology for the anti-Platelet Factor 4 Heparin anti-body
- Enhance the clinical awareness of Platelet Factor IV Antibodies
  - Population at risk
  - Clinical signs
  - Diagnosis and treatment
  - Importance of protocol
  - Medical Consequences of Poor Quality
  - Patient Satisfaction

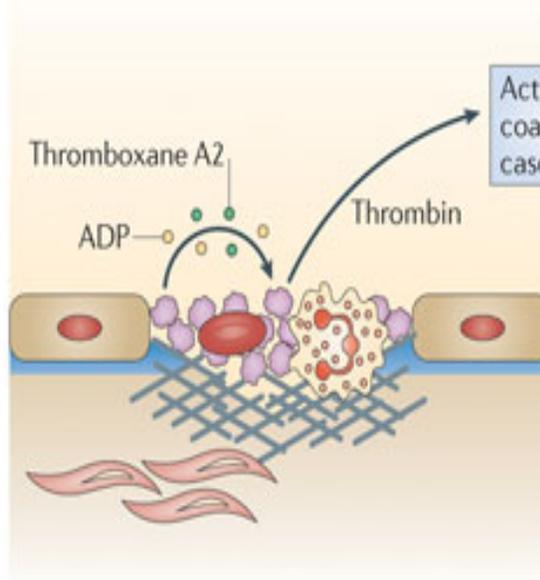




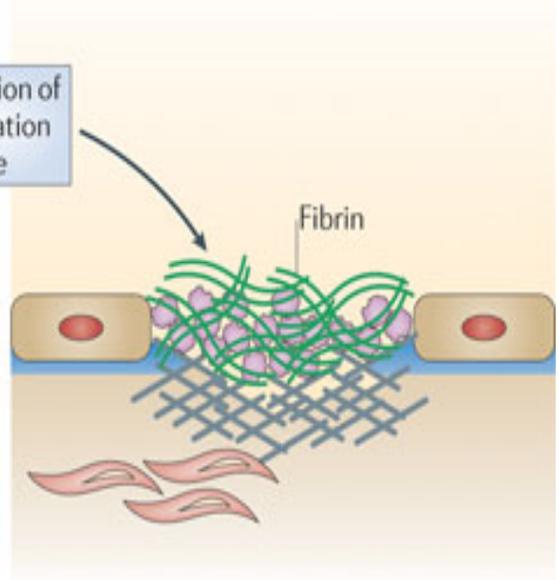
### Platelets adhere to site of vascular injury



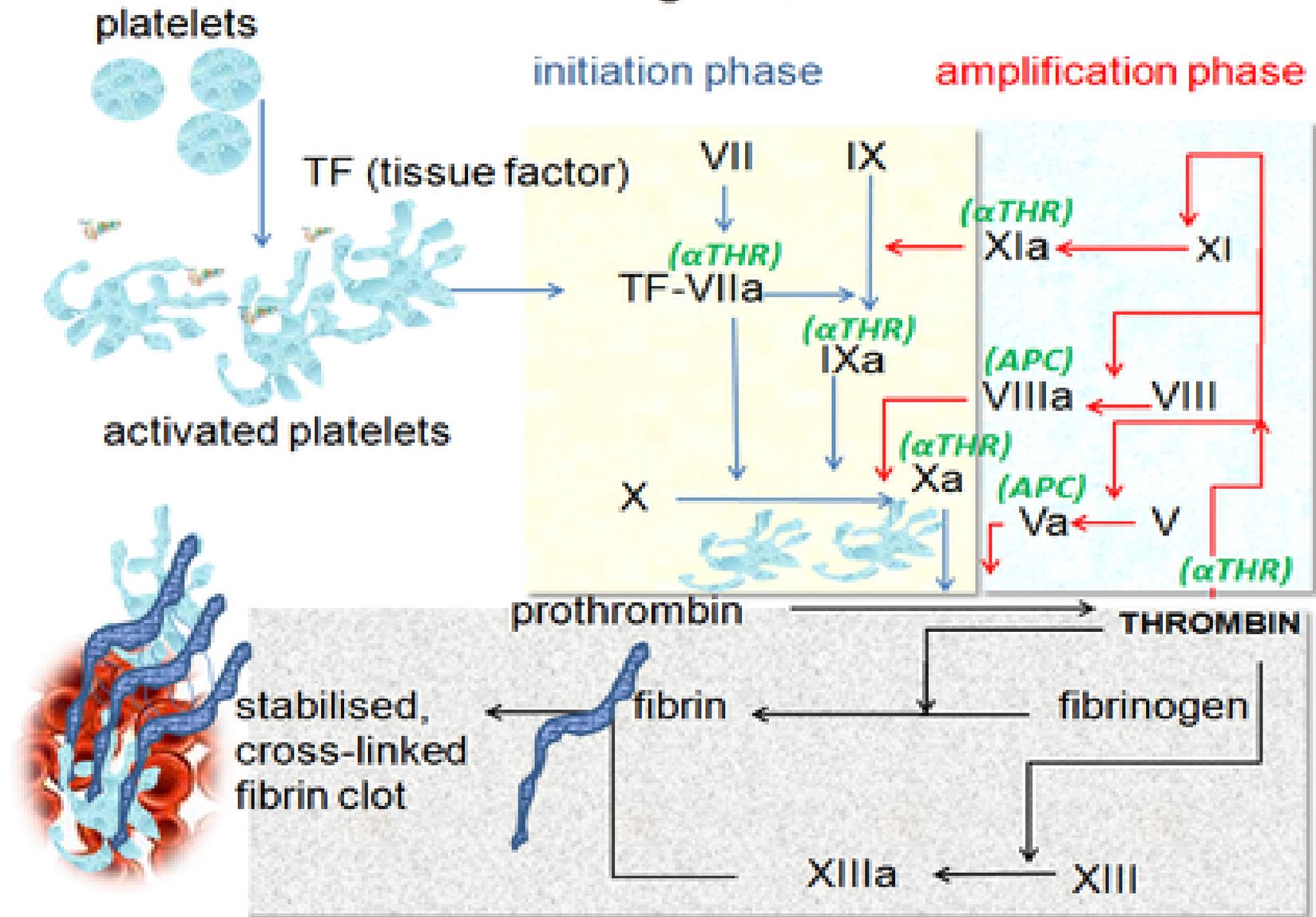
### Platelet aggregation and activation

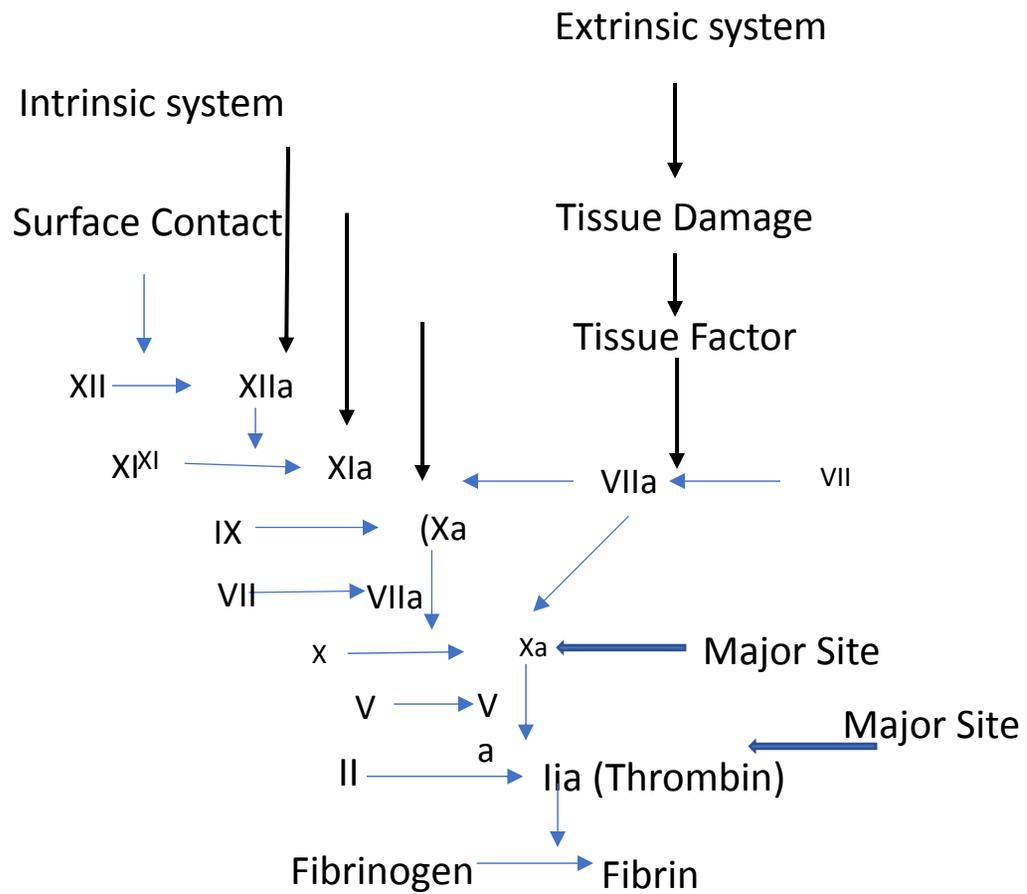


### Haemostatic plug formation



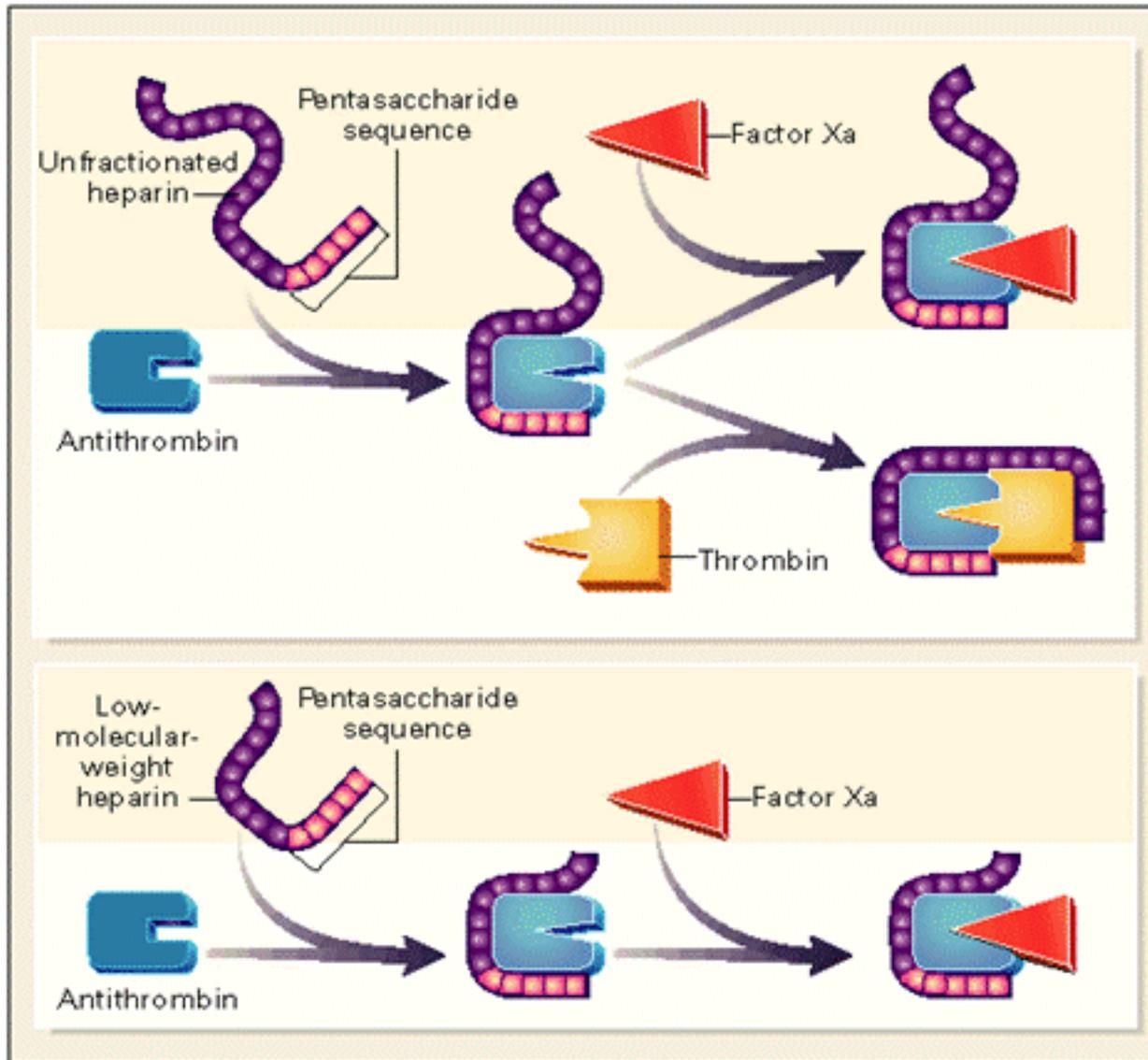
# Blood coagulation *in vivo*



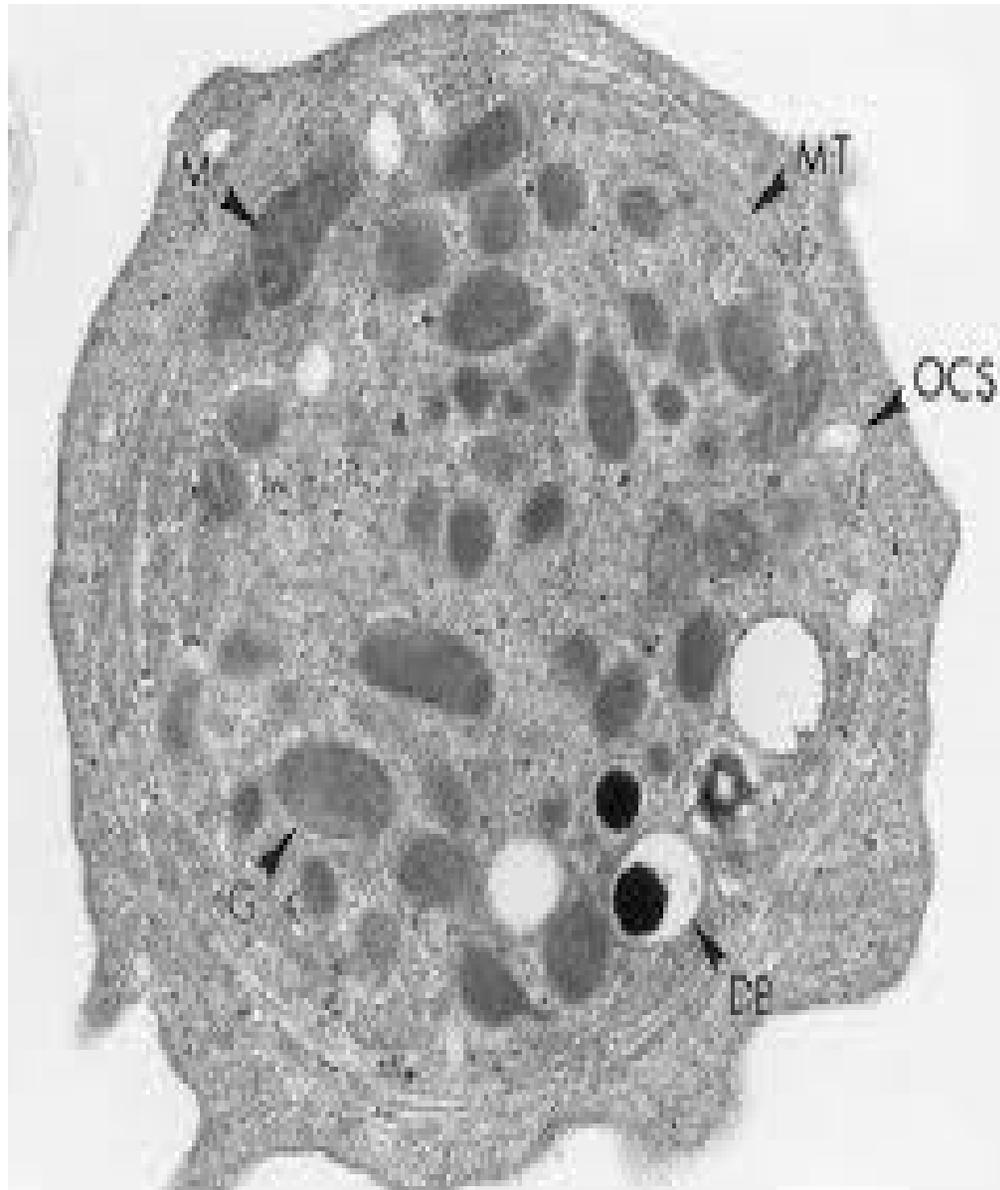


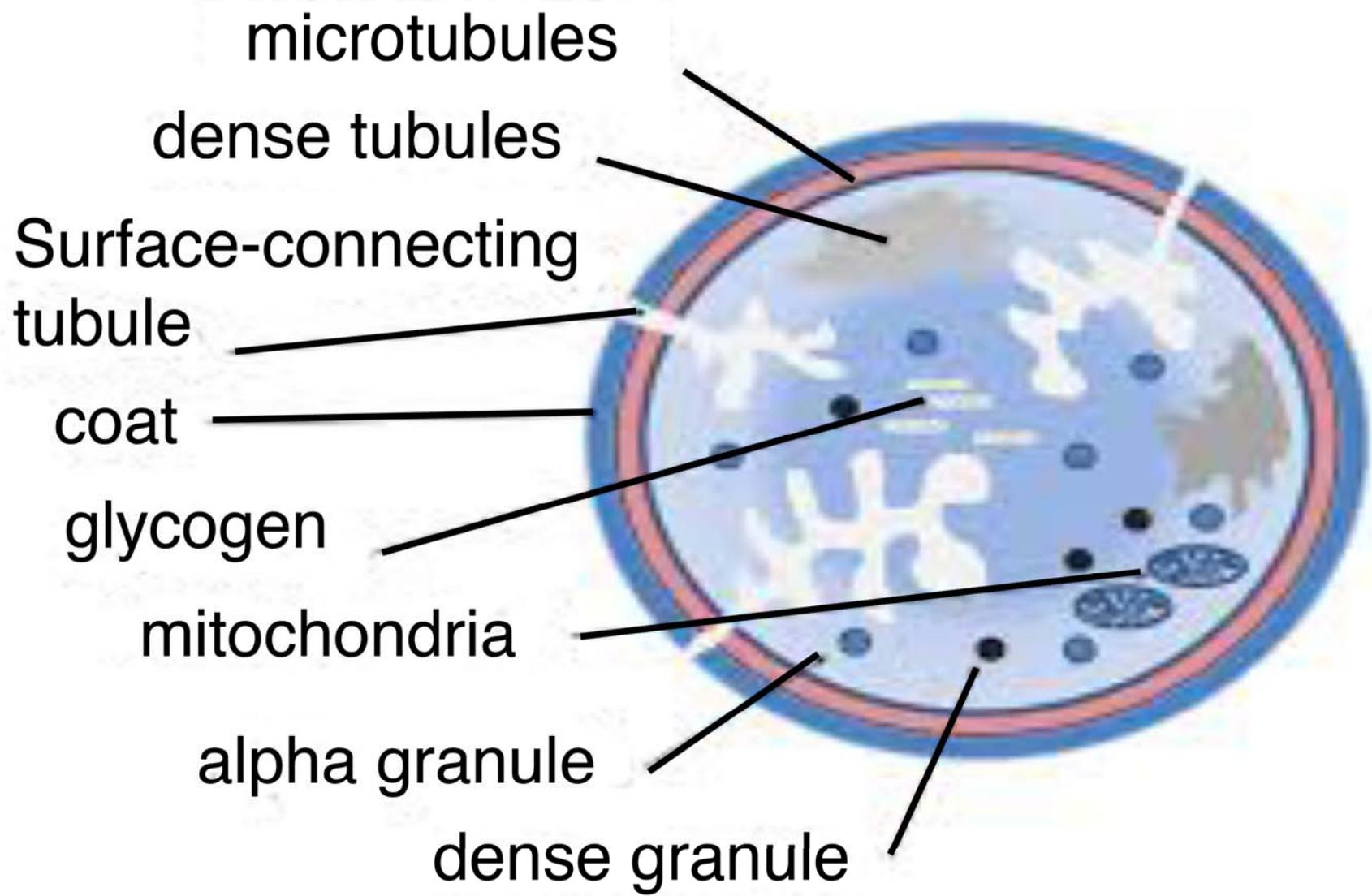
# Mechanism of Action

Heparin



LMWH





# CASE STUDY

- 57 year old female admitted with pneumonia and respiratory failure
- Admission platelet count was 230,000
- Prophylactic heparin administered
- On the 7<sup>th</sup> ICU day, the patient arrested
- Platelet count 110,000

## Result

**Patient expired**

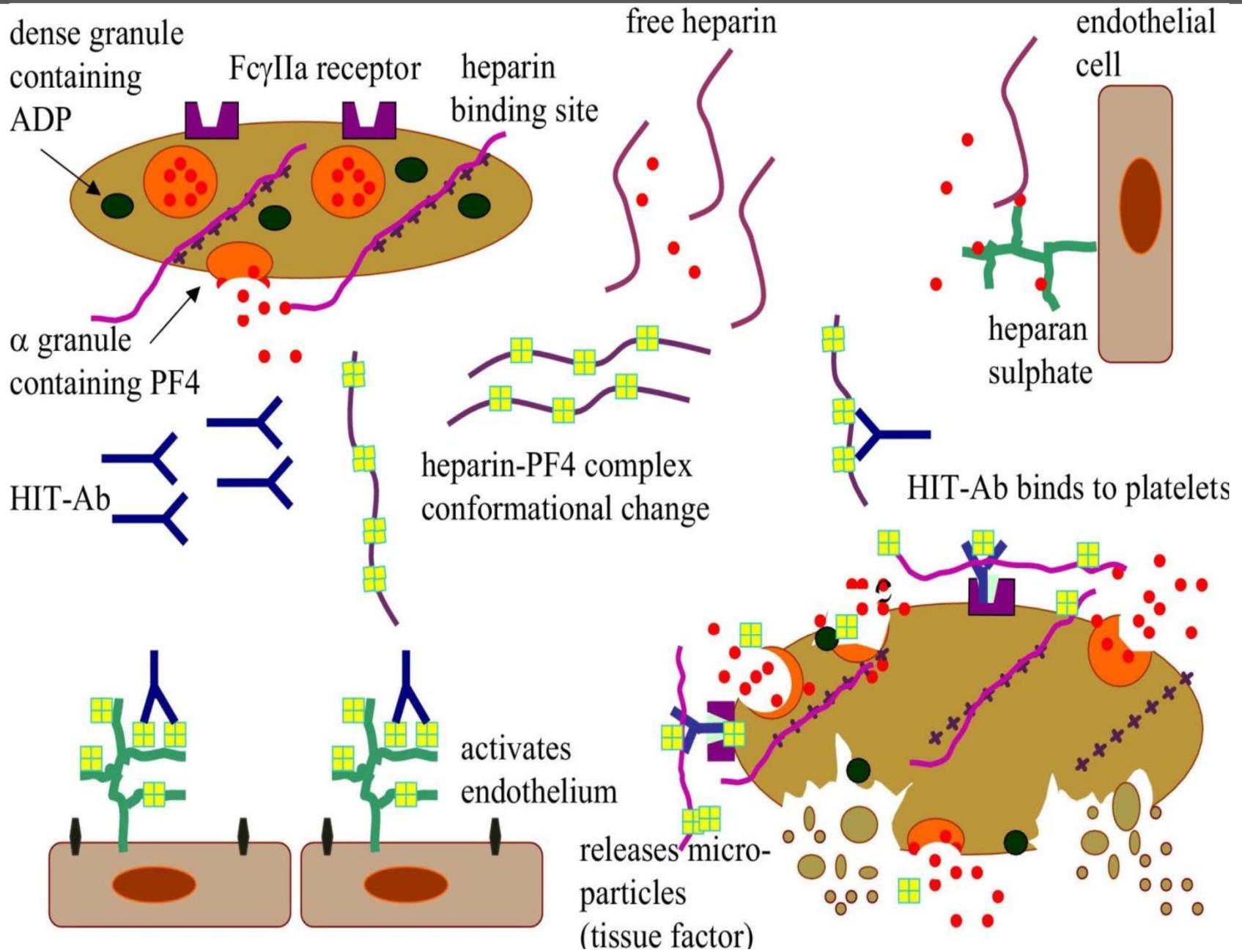
**Diagnosis-Heparin Induced Thrombocytopenia HIT**

# Heparin Induced Thrombocytopenia

- Most common adverse event with heparin use is bleeding.
- Some patients develop a pro-thrombotic state known as heparin induced Thrombocytopenia (HIT)
- HIT Type I: Mild asymptomatic decrease in platelet count
- HIT Type II: Severe, potentially devastating thromboembolic complication; life and limb threatening

# Heparin Induced Thrombocytopenia Type II

- An immune complex can form between heparin and platelet Factor 4 (PF4) released by platelets. This complex becomes an antigen and elicits an antibody response.
- The antibody response destroys the platelets
- Observed in 2-5% of patients treated with heparin
- The risk of thrombosis is 33-50%



# Clinical Signs of HIT

- Deep venous thrombosis (50%)
- Pulmonary Embolism (25%)
- Skin lesions at injection site (10-20%)
- Acute limb ischemia (5-10%)
- Warfarin associated limb gangrene (5-10%)
- Acute CVA or myocardial infarction (3-5%)

# Patient Population

- Cardiopulmonary Bypass Surgery and Orthopedic Surgery are greatest risks
- HIT may also occur through:
  - Heparin flushes or subcutaneous administration
  - Heparin-coated catheters and prosthesis
  - Chronic dialysis patients

# Factors Influencing the Frequency of HIT

- Type of Heparin and route of administration Bovine UFH>Porcine UFH>LMWH Intravenous>subcutaneous
- Patient Population
- Duration of heparin therapy-use beyond day 5 increases the risk of HIT
- Sex: Female>Male

# Probability of HIT

- 50% fall in platelet count
- Onset between 5 and 10 days after therapy or <1 day if heparin administered within 100 days
- New thrombosis or thrombotic signs

# The Diagnosis of HIT-The four Ts

1. Thrombocytopenia
2. Timing of Platelet count
3. Thrombosis
4. Other causes of thrombocytopenia

## HIT Type II-Clinico-Pathologic Diagnosis

- >50% platelet fall from Baseline or <100,000/ml.
- Onset varies-typical 5-10 days after heparin exposure; rapid < 1 day of UFH re-exposure (prior exposure within 100 days); delayed-up to 40 days after UFH exposure
- New thrombosis, skin necrosis
- No other causes
- Antibodies to complexes of HPF4

# Laboratory Diagnosis of HIT

- Platelet Count
- H-PF4 antibody check
- Platelet Functional Analysis

# Antigen-Base Tests

- Standardized Reagents
- Not dependent on platelet donors
- Direct testing for Anti-Platelet Factor IV antibody is available as a stat test with results in 10 minutes

# Treatment of HIT

- Discontinue heparin
- Delay Warfarin until platelet count recovers
- Avoid platelet transfusion
- Treat with direct thrombin inhibitors, e.g. argatroban(Acova), bivalirudin

# Conclusions

- HIT is a clinical and laboratory Diagnosis
- Patients with HIT are at risk for life and limb threatening thrombotic disease
- In critically ill patients, a negative antigen test paired with the 4T's can exclude the presence of anti-PF4 antibodies

## Elisa Vs Immuno Precipitation

- Elisa is a two step method versus a one step immuno precipitation method.
- Immuno precipitation can be performed in less than one hour.