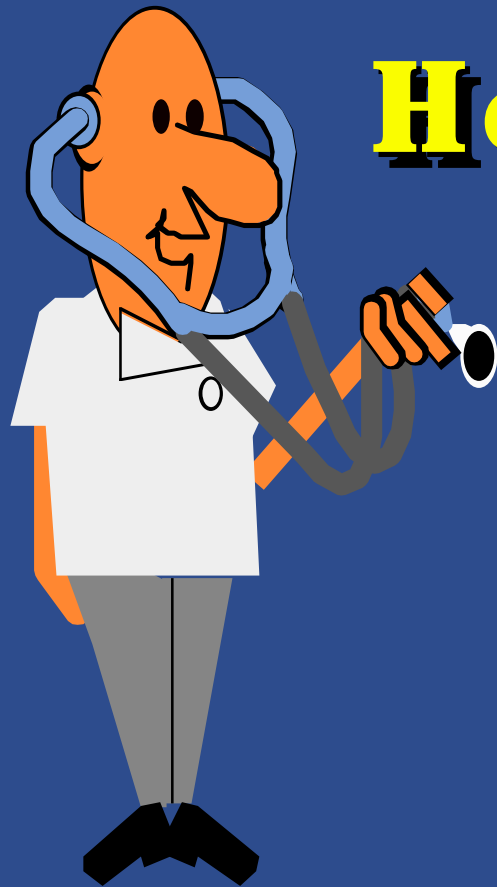


# Case Studies in Clinical Hemostasis



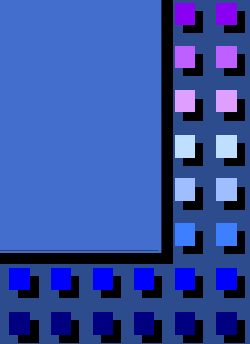
**Case #2**  
**The Case of the 38 Year-Old**  
**Woman with**  
**Post-Operative DVT**

# **Patient A.K.**

- **38 year-old woman**
- **Admitted for hysterectomy**
- **Normal preoperative laboratory studies**
- **Surgery uneventful**
- **Day 3 - RLE pain and swelling, IV heparin started**
- **Day 8 - RUE pain, cool and dusky, decreased pulses**
- **Right radial artery thrombosis found**
- **Platelet count - 40,000/ $\mu$ L**



## **Patient A.K.**

- **What is the most likely etiology of the thrombosis ?**
  - **What immediate action should be undertaken ?**
  - **What additional laboratory assays should be requested ?**
- 

# Case Studies in Clinical Hemostasis



**Case #2**  
**Heparin-Induced**  
**Thrombocytopenia**

# Heparin

- Polysaccharide chains of glucosamine, glucuronic and iduronic acid covalently linked to a polypeptide matrix (heparin proteoglycan)
- Found in liver and mast cells
- Isolated from liver in 1916 by McLean
- First used as anticoagulant in 1940s
- Responsible for more drug induced complications than any other hospital drug
- Bleeding is most common problem
- Thrombocytopenia + thrombosis is frequently misdiagnosed

**MORE THAN ONE  
TRILLION  
UNITS OF HEPARIN  
ARE USED IN THE  
U.S. EACH YEAR**



# Heparin-Induced Thrombocytopenia

- **Platelet clumping**

  - HIT Type I**

    - Mild, very common, non-immunologic origin**
    - 25-30% of heparinized blood specimens**

- **HIT with thrombosis syndrome (HITTS)**

  - HIT Type II (“White clot syndrome”)**

    - Rare, severe (PLT < 100,000/ $\mu$ L), immunologic**
    - Independent of heparin dose**

    - 0.5 - 5% incidence, 5-22 days after onset**

    - High incidence of morbidity and mortality**

    - Risk factors - Multiple heparin exposures,  
vascular disease, vascular injury**

    - Cardiothoracic surgery patients at greatest risk**

# Drug-Induced Thrombocytopenia



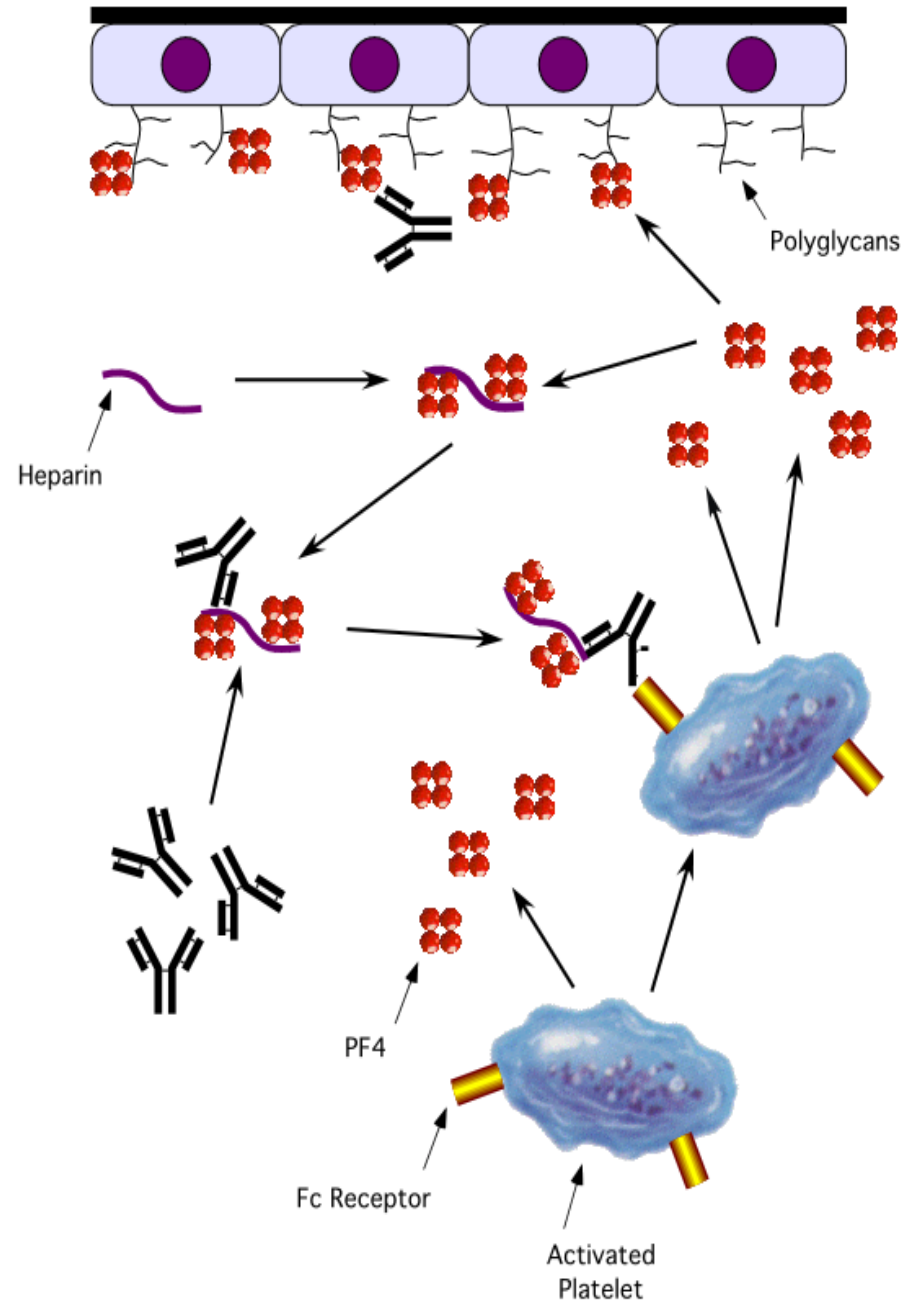
From Hoffbrand and Pettit  
Color Atlas of Clinical Hematology  
Mosby-Wolfe, 1994

# Heparin-Induced Thrombocytopenia



# HIT Mechanism

- 1. Injected heparin reacts with PF4**
- 2. IgG antibodies bind to heparin/PF4 complexes to form immune complexes (ICs)**
- 3. Immune complexes bind to PLT receptors, activated PLTs formed**
- 4. Activated PLTs release more PF4, new ICs formed, thrombocytopenia occurs**
- 5. Excess PF4 binds to glycosaminoglycans on endothelial cells**
- 6. Abs bind to endothelial cells, causing antibody-mediated endothelial injury**
- 7. Thrombosis and DIC occurs**



# Diagnosis of HIT

- **Platelet aggregation**

  - Aggregation of control PLTs by patient's serum in the presence of heparin**

  - Easy to perform, poor sensitivity and specificity**

- **Serotonin release assay**

  - Release of serotonin from control PLTs during aggregation**

  - Antibodies in serum of HIT patients causes PLT activation and serotonin release**

  - Serotonin-radiolabeled PLTs used**

  - Expensive, difficult to perform**

- **Heparin/PF4 ELISA**

  - Microtiter trays with immobilized heparin/PF4 complexes**

  - Extremely sensitive, ? specificity**

# Treatment of HIT

## ■ Stop heparin!

## ■ Alternative anticoagulants

Warfarin, low-molecular weight heparin, ancrod, aspirin

## ■ Anti-thrombin agents

Refludan [lepirudin (rDNA)] recently approved for Rx

Recombinant hirudin derived from yeast cells

Highly specific direct inhibitor of thrombin

Mode of action independent of antithrombin III

## ■ Adjunctive therapy

Plasmapheresis, thromboembolectomy

# Case Studies in Clinical Hemostasis



**Case #2**  
**The End**