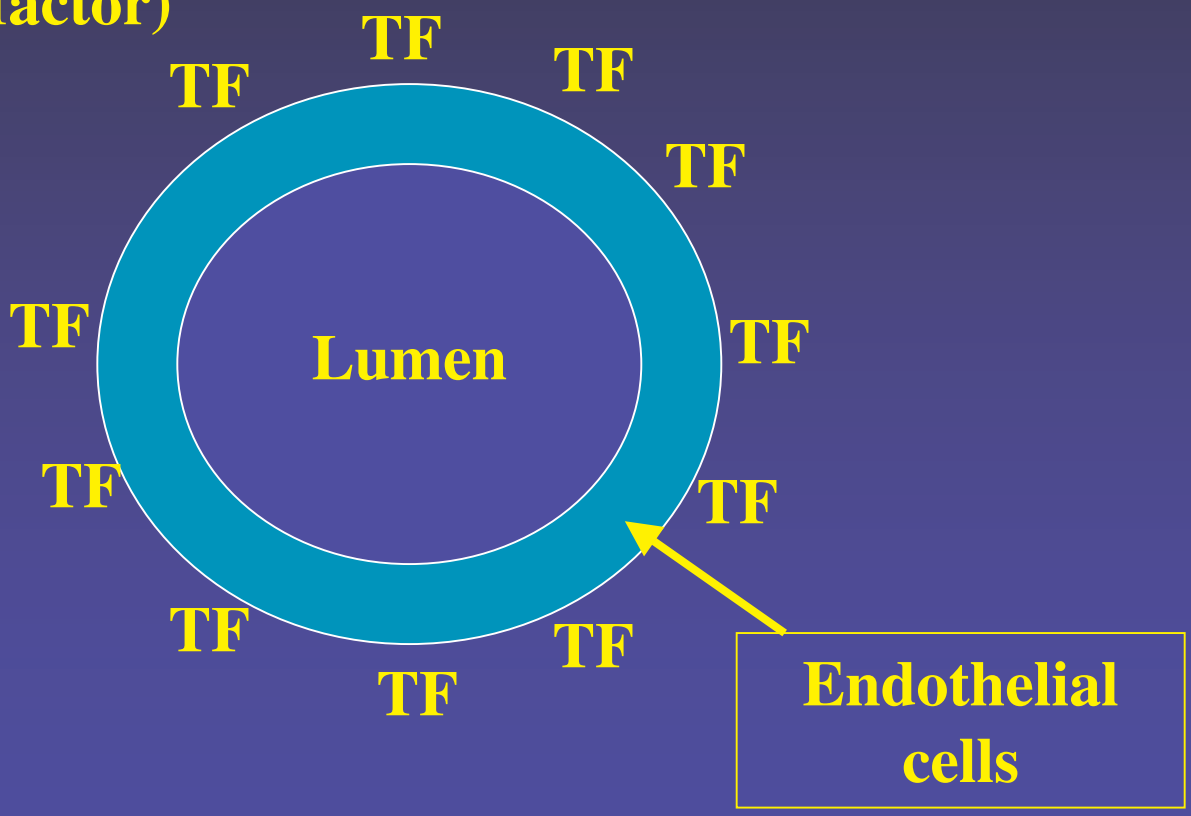
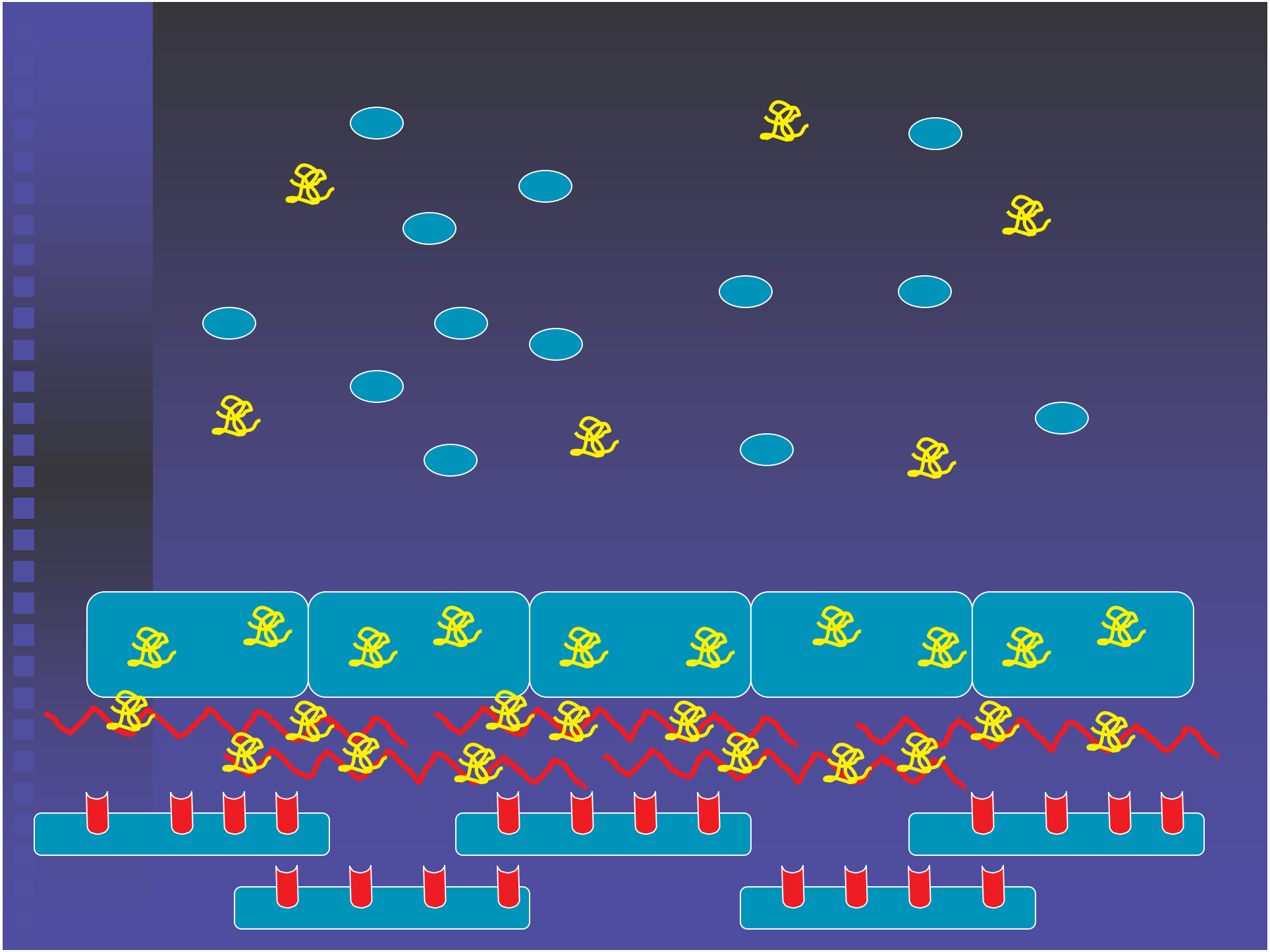
Inherited bleeding disorders and pregnancy

Blood vessel structure

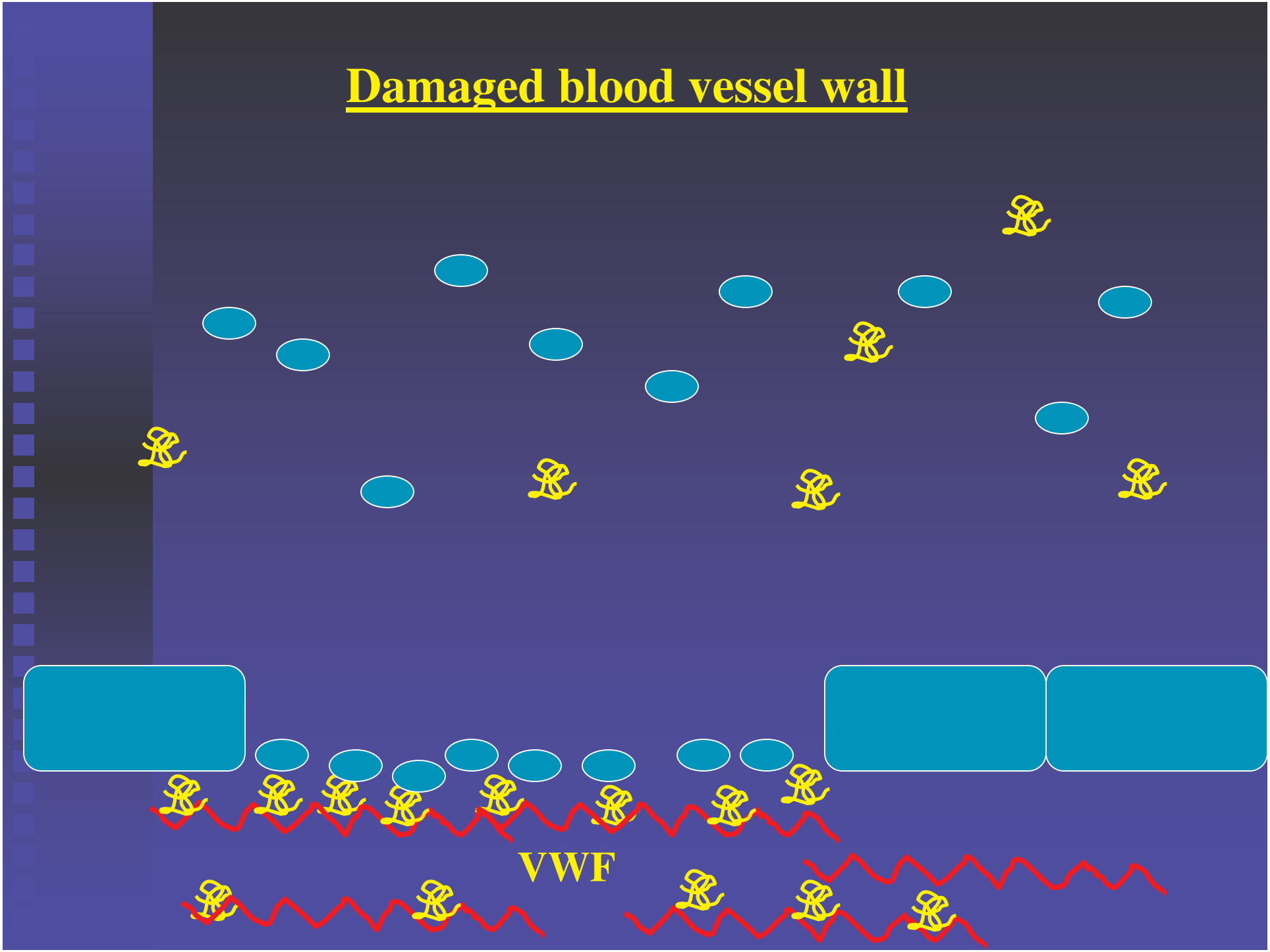
Subendothelial matrix

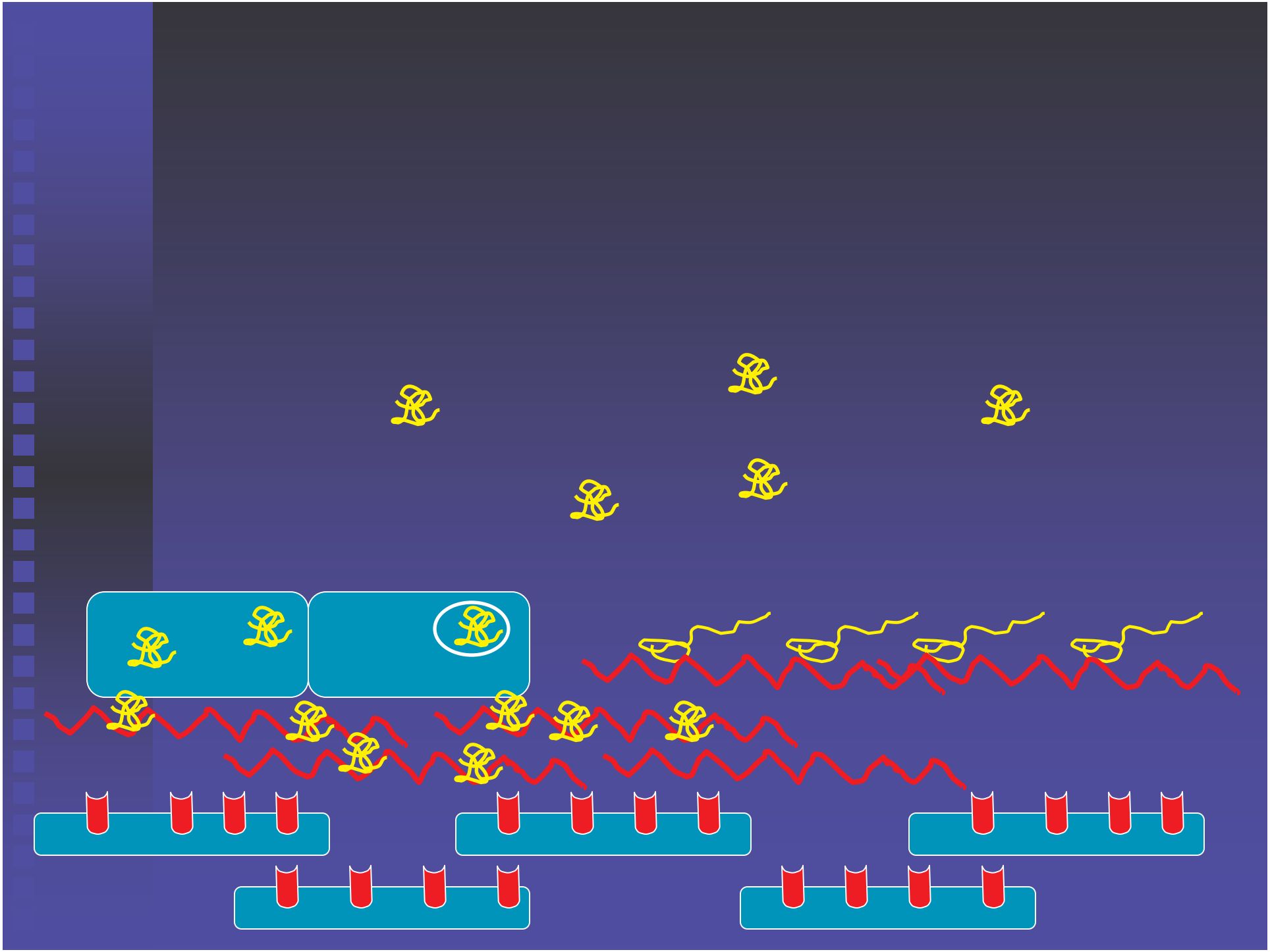
(collagen and tissue factor)

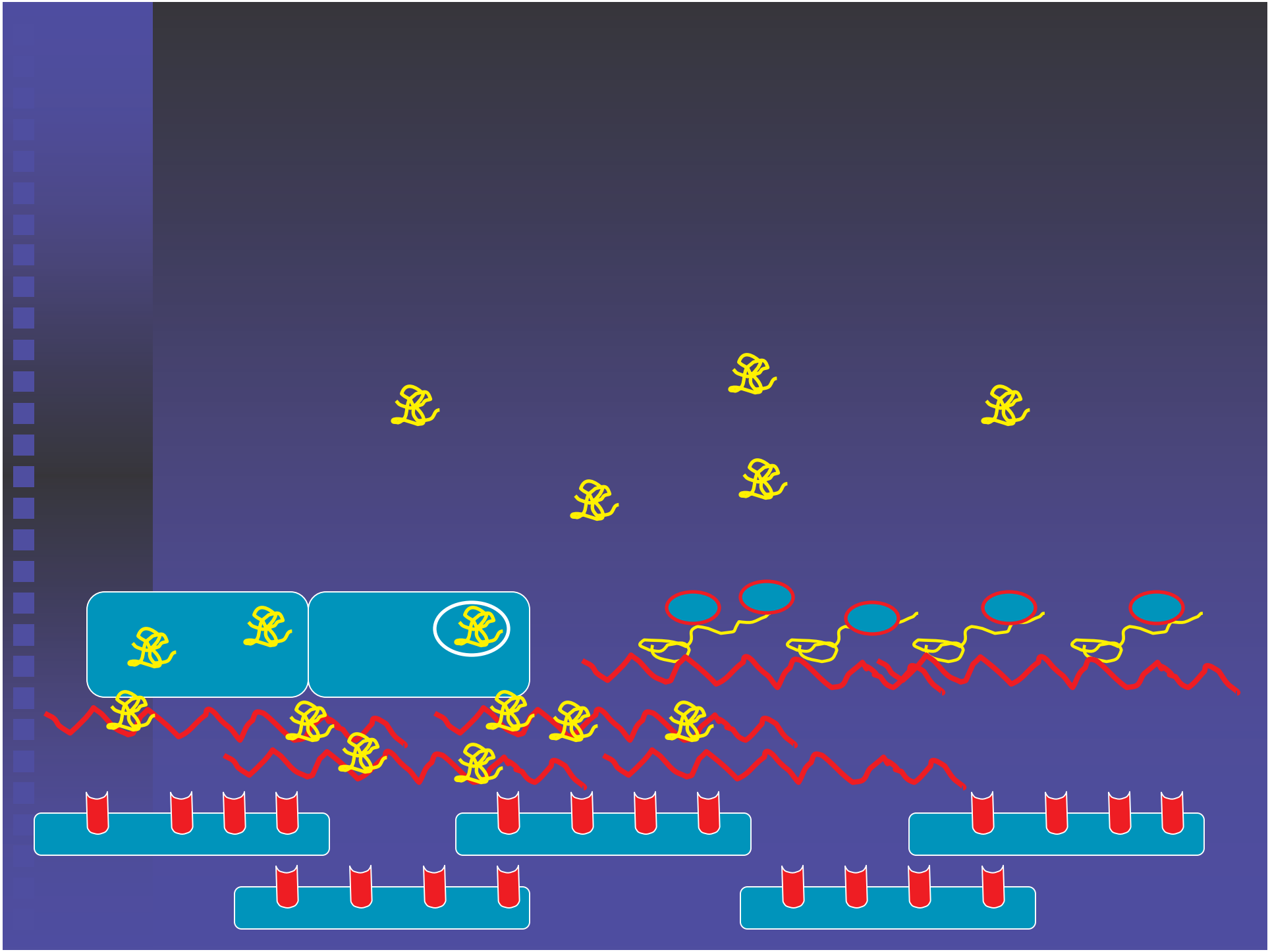


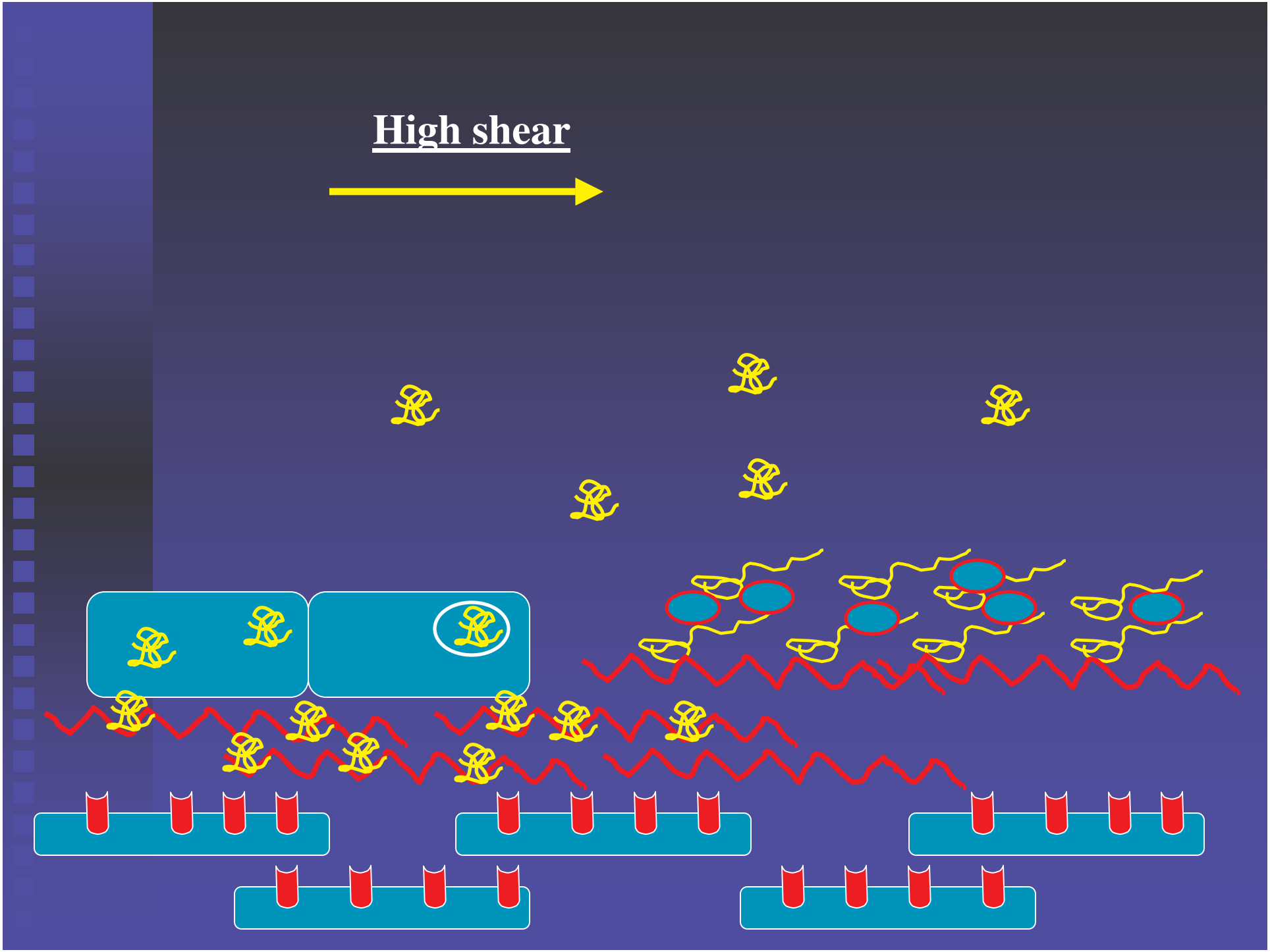


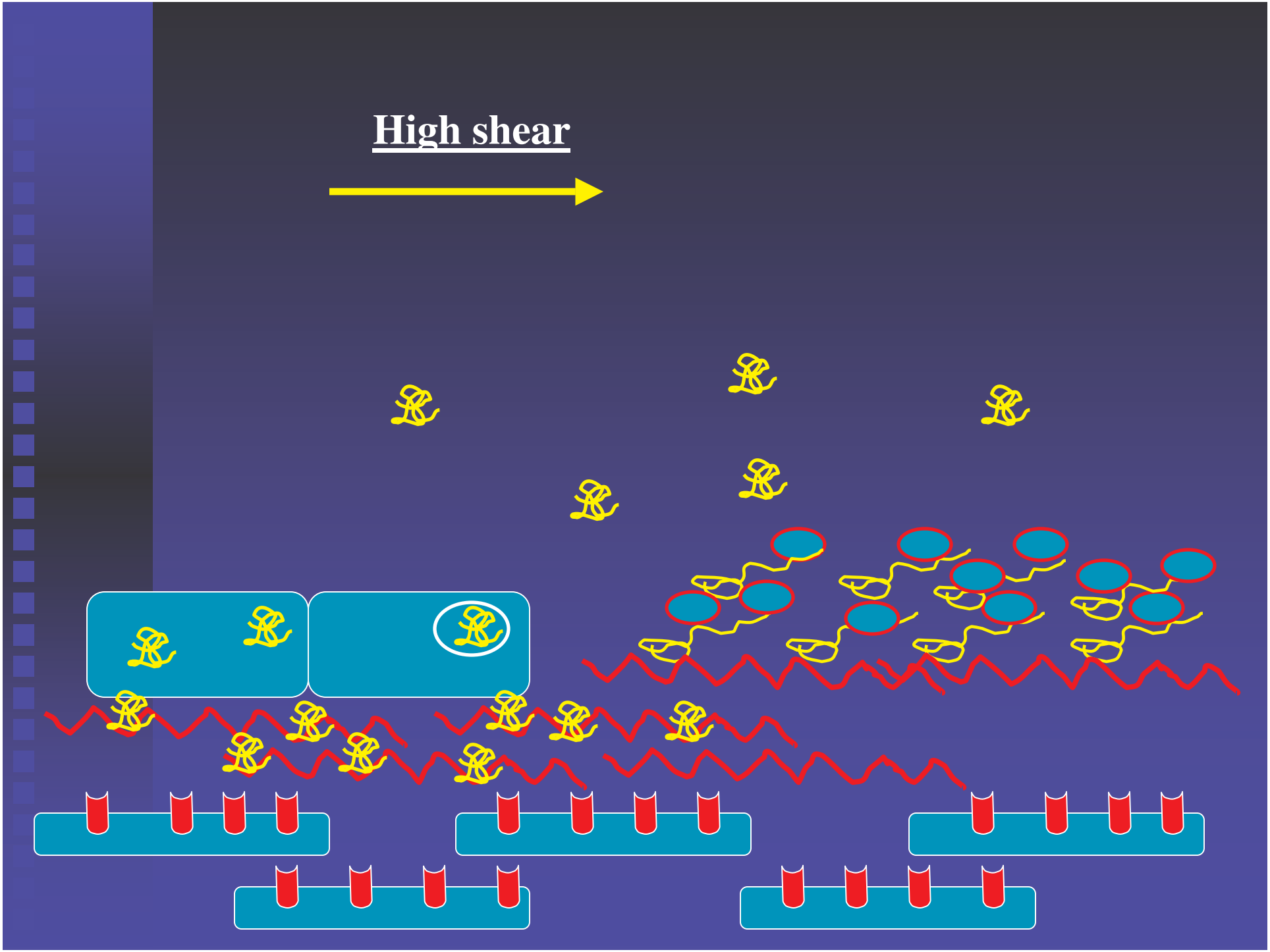
Damaged blood vessel wall

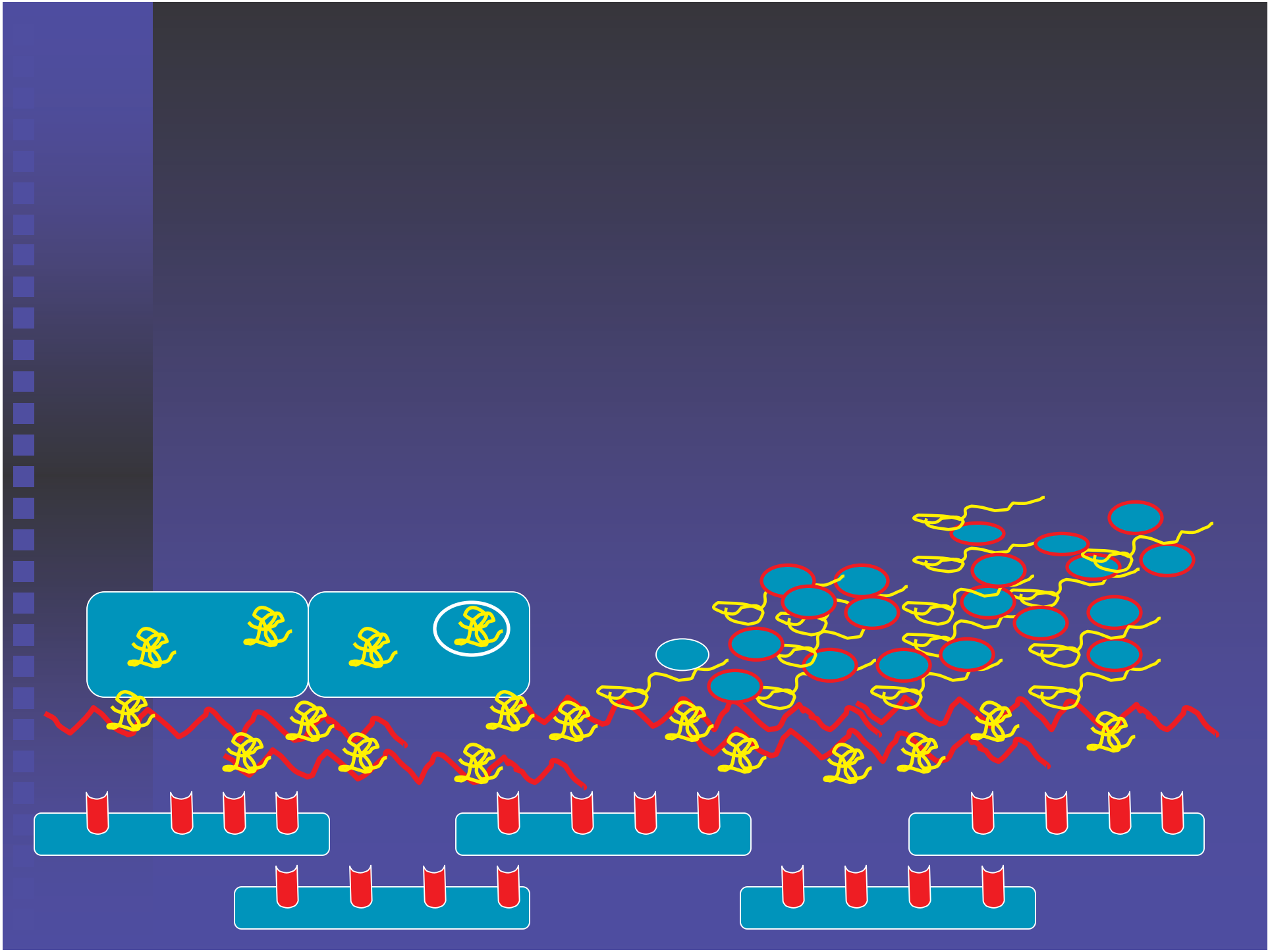







High shear

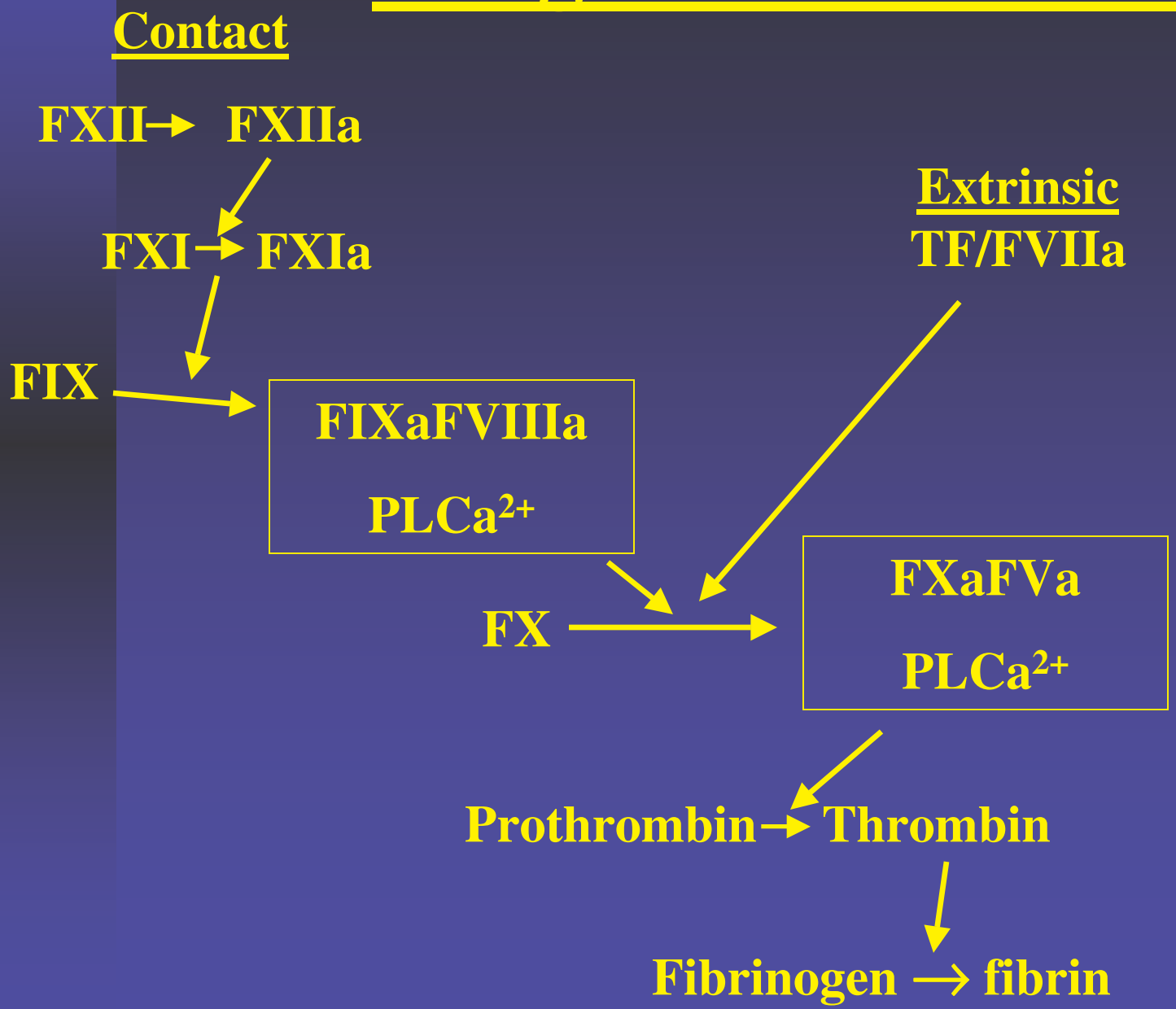

High shear

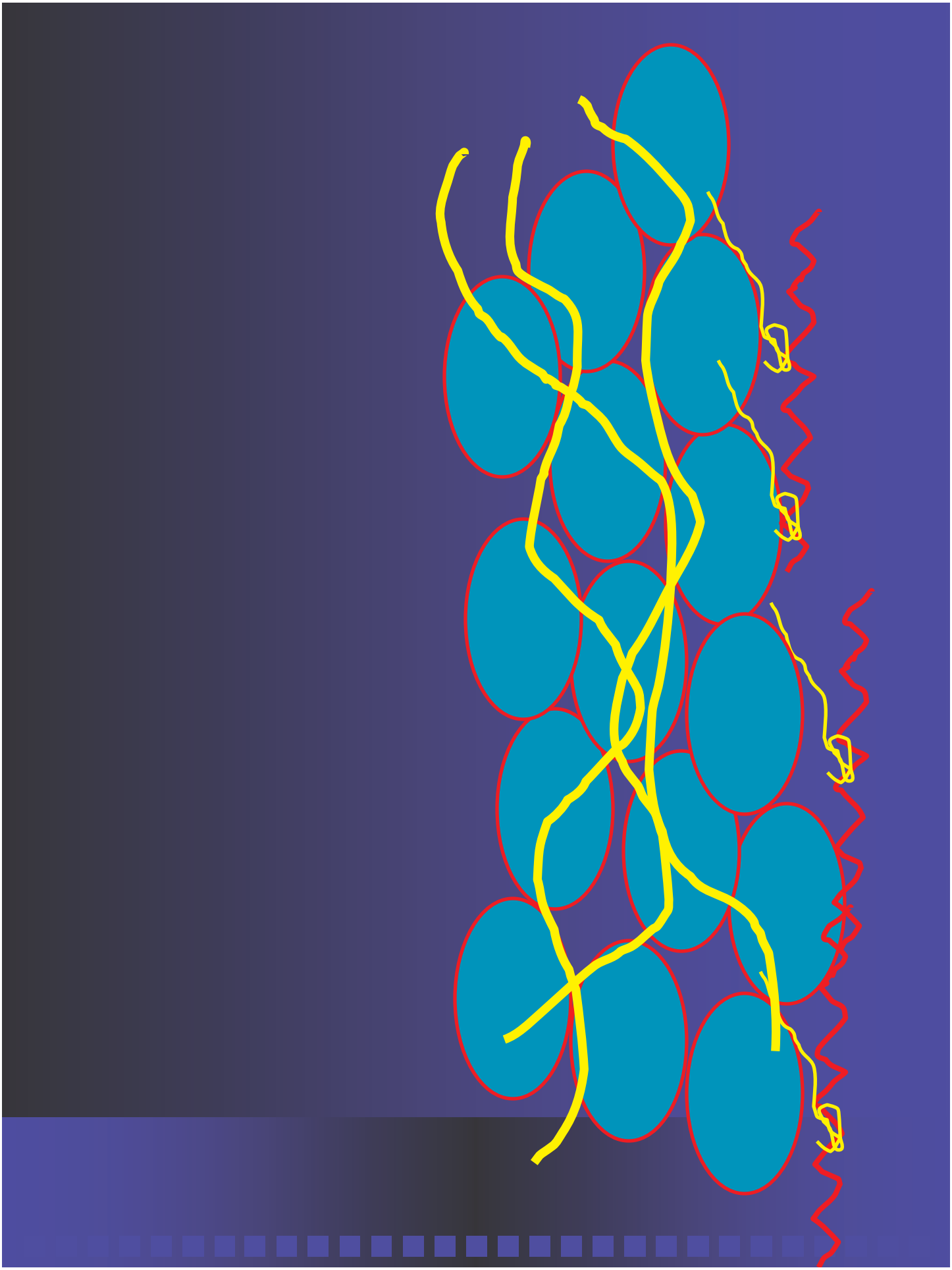


Stabilisation of platelet plug

- Platelet plug stablised by fibrin clot
- Fibrin end product of coagulation cascade

Coagulation cascade





Inherited bleeding disorders

- **Disorders of platelet plug formation**
  - **Von Willebrand disease**
  - **Platelet function defects**
- **Typical bleeding**
  - **Mucosal bleeding**
  - **Menorrhagia, epistaxis,**
  - **Post partum haemorrhage**
  - **Bleeding from invasive procedures**
    - **Ceasarian section**
    - **Epidural**

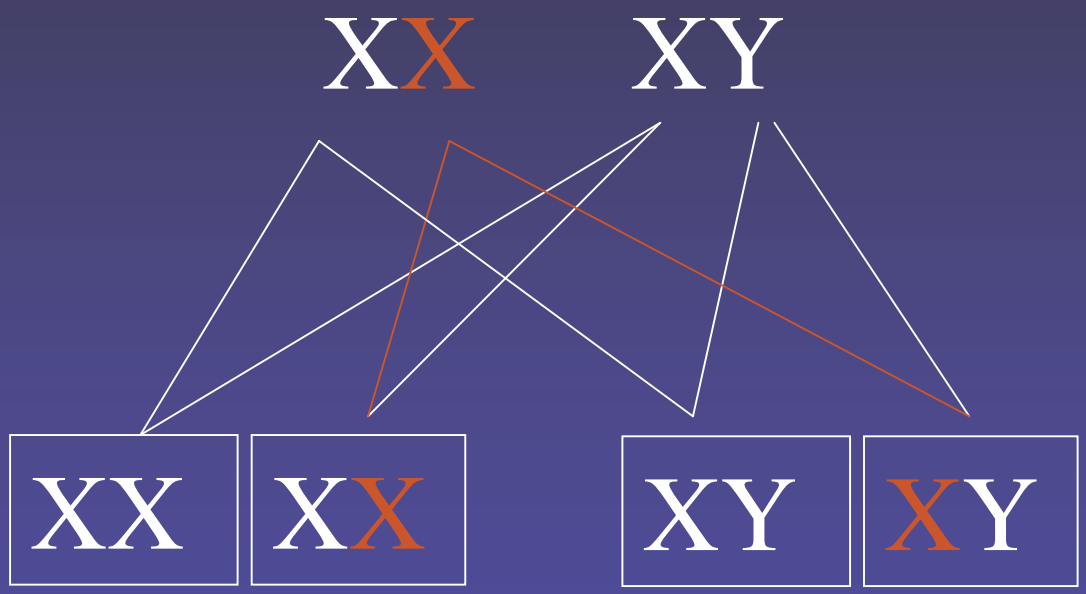
Inherited bleeding disorders

- **Disorders of fibrin clot formation**
  - **Haemophilia A and B**
  - **Other factor deficiencies**
- **Typical bleeding**
  - **Joint and muscles**
  - **Deep tissue bleeds (intracranial, retroperitoneal)**
  - **Cephalohaematoma**

Inheritance of bleeding disorders

- **Haemophilia**
  - **X-link recessive**
- **Von Willebrand disease**
  - **Autosomal dominant**

Inheritance of haemophilia



Issues

- Diagnosis of carriers of bleeding disorders
- Genetic counselling and reproductive options
- Maternal haemostasis:
  Delivery, anaesthesia, LSCS, PPH
- Neonatal haemostatic management
- Blood product exposure
  Transfusion transmitted disease
  Maternal
  Fetal

Haemophilia A and B

- Carrier detection and diagnosis
  - Tracing (effect of HIV)
  - Confirm family disease
  - Confirmation
    (gene tracking/mutation analysis)
  - Genetic counselling
- Measure factor level

Reproductive options

- Chance/adoption/no children
- Antenatal diagnosis by CVS
- Amniocentesis
- Umbilical vein sampling
- Pre-implantation sexing
- Pre-implantation diagnosis
- Fetal DNA from maternal blood
- HIV issues (partner testing/sperm washing/decreasing partner exposure/prognosis)

Antenatal care in haemophilia A and B

- Fetal sexing by ultrasound
- Monitor maternal factor level
  FVIII increases
- Education of parents
- Consent to treatment
- Close joint antenatal care

Management of delivery of haemophilia A and B

- Haemophilia specialist immediately available
- Maternal haemostasis
  - Know factor level
  - Vaginal delivery/LSCS/epidural
  - Factor concentrates
  - DDAVP
- Neonatal haemostasis
  - No ventouse, avoid forceps and fetal scalp monitoring
  - Immediate blood sample for diagnosis
  - Consider factor concentrate at birth

Erik Von Willebrand


multimap
NORWAY
Bergen
OSLO
HELSINKI
Saint Petersburg
TALLINN
STOCKHOLM
ESTONIA
Goteborg
RIGA
LATVIA
DENMARK
Odense
KOBENHAVN
LITHUANIA
Gdansk
VILNIUS
MINSK
Hamburg
BELARUS

Von Willebrand disease

- Abnormal von Willebrand factor
- Primary haemostasis
  - Platelet adhesion and aggregation
  - Mucosal and immediate wound bleeding
- Secondary haemostasis
  - Stabilises factor VIII
  - Delayed bleeding, poor wound healing

Type 1 VWD

- Type 1 VWD
  - Low level of normal VWF/VIII
  - Bleeding: mucosal
- VWF and FVIII increase in pregnancy
  - Rarely bleeding at delivery
- VWF/FVIII falls rapidly after delivery
  - Late PPH
  - Treatment: DDAVP
- Inheritance unpredictable
- Neonate usually normal levels

Type 2 VWD

- Type 2A and 2M
  - Dysfunctional VWF
  - Factor VIII may be normal
  - Significant loss of primary haemostasis
- Increase level in pregnancy but still dysfunctional
- Predictable inheritance
- Neonate may be significantly affected
- Mother and baby may need urgent VWF concentrate (NB thrombosis)

VWD subtypes

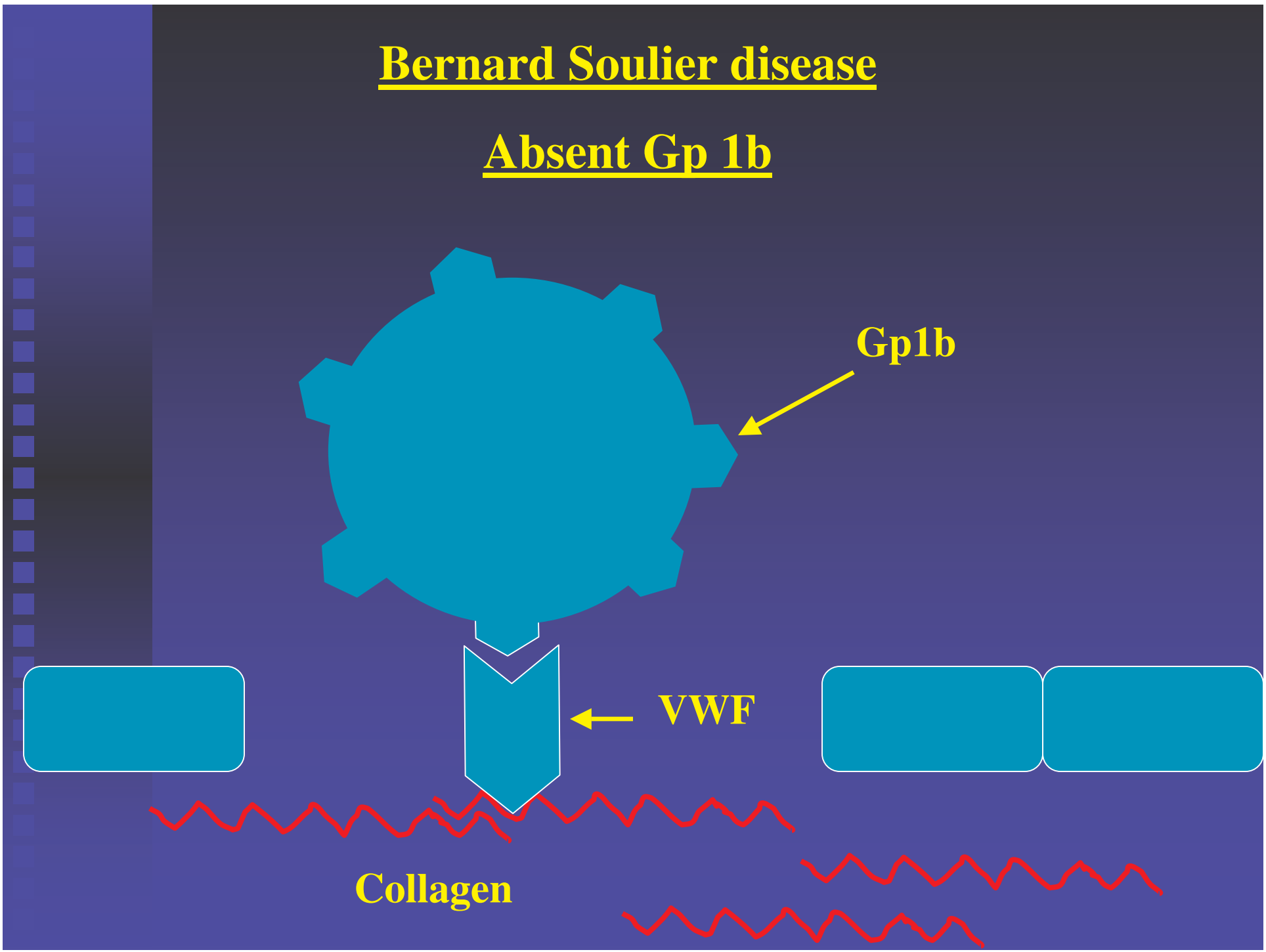
- Type 3
  - Undetectable VWF very low FVIII
  - Very high risk of uncontrollable bleeding at delivery
  - Potentially life-threatening
- Treatment with VWF concentrate mandatory
  - Close laboratory monitoring

Platelet function disorders

- Glanzmann's thrombasthenia
- Bernard Soulier disease

Bernard Soulier disease

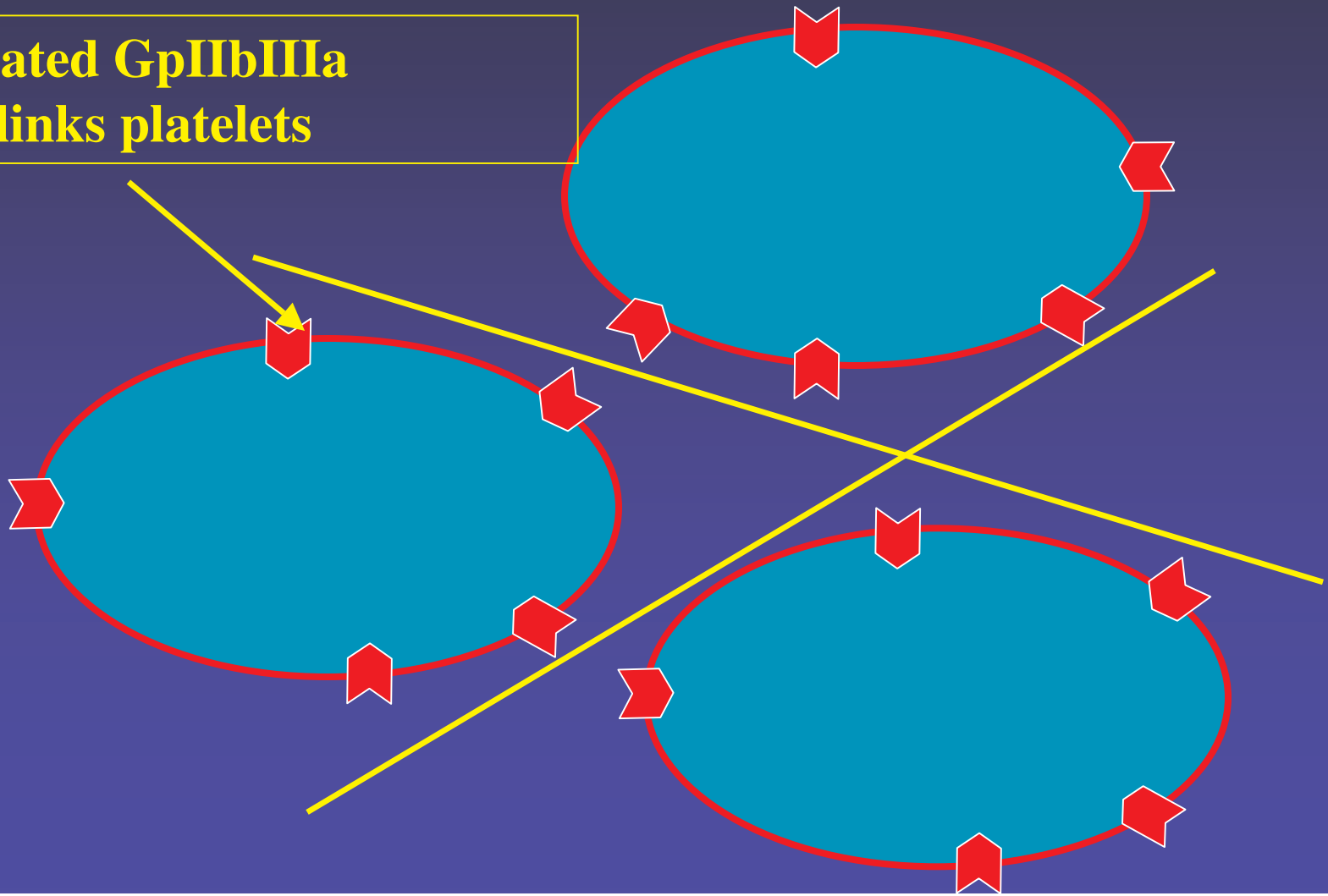
Absent Gp 1b



Glanzmann's thrombasthenia

Absent GpIIbIIIa

Activated GpIIbIIIa crosslinks platelets



Platelet function disorders

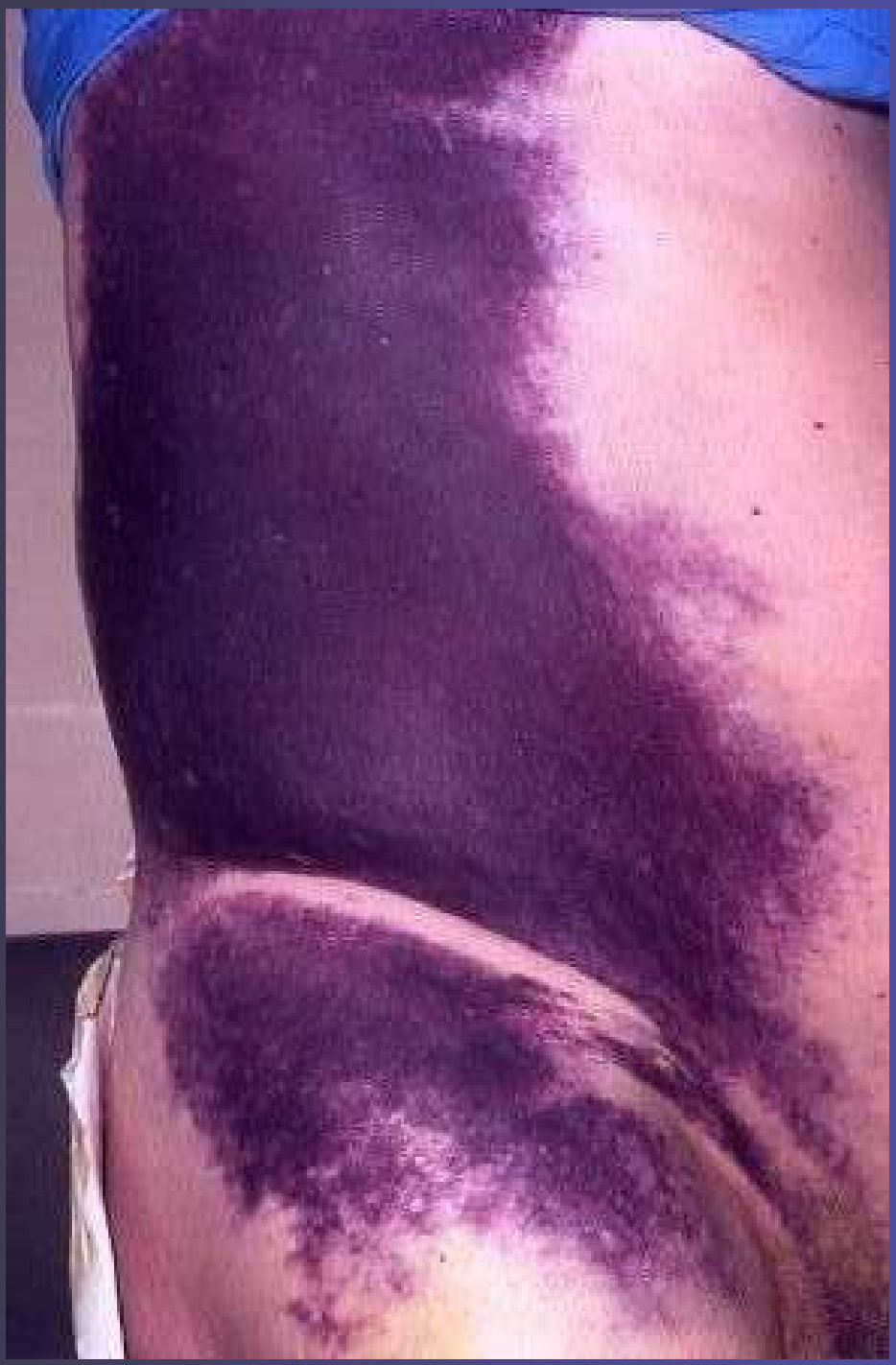
- High risk of uncontrollable bleeding
  Life-threatening bleeding predictable
- Autosomal recessive
  - Neonate not affected
- Treatment
  Highly specialised
  Platelets (HLA-matched)
  rFVIIa

Dysfibrinogenaemia

- Relatively common
  - Third bleed
  - Third thrombosis
  - Third asymptomatic
- Treatment considerations
  - Thromboprophylaxis
  - Fibrinogen concentrate
- Close clinical observation is key

Acquired haemophilia A

- Auto antibody against factor VIII associated with pregnancy

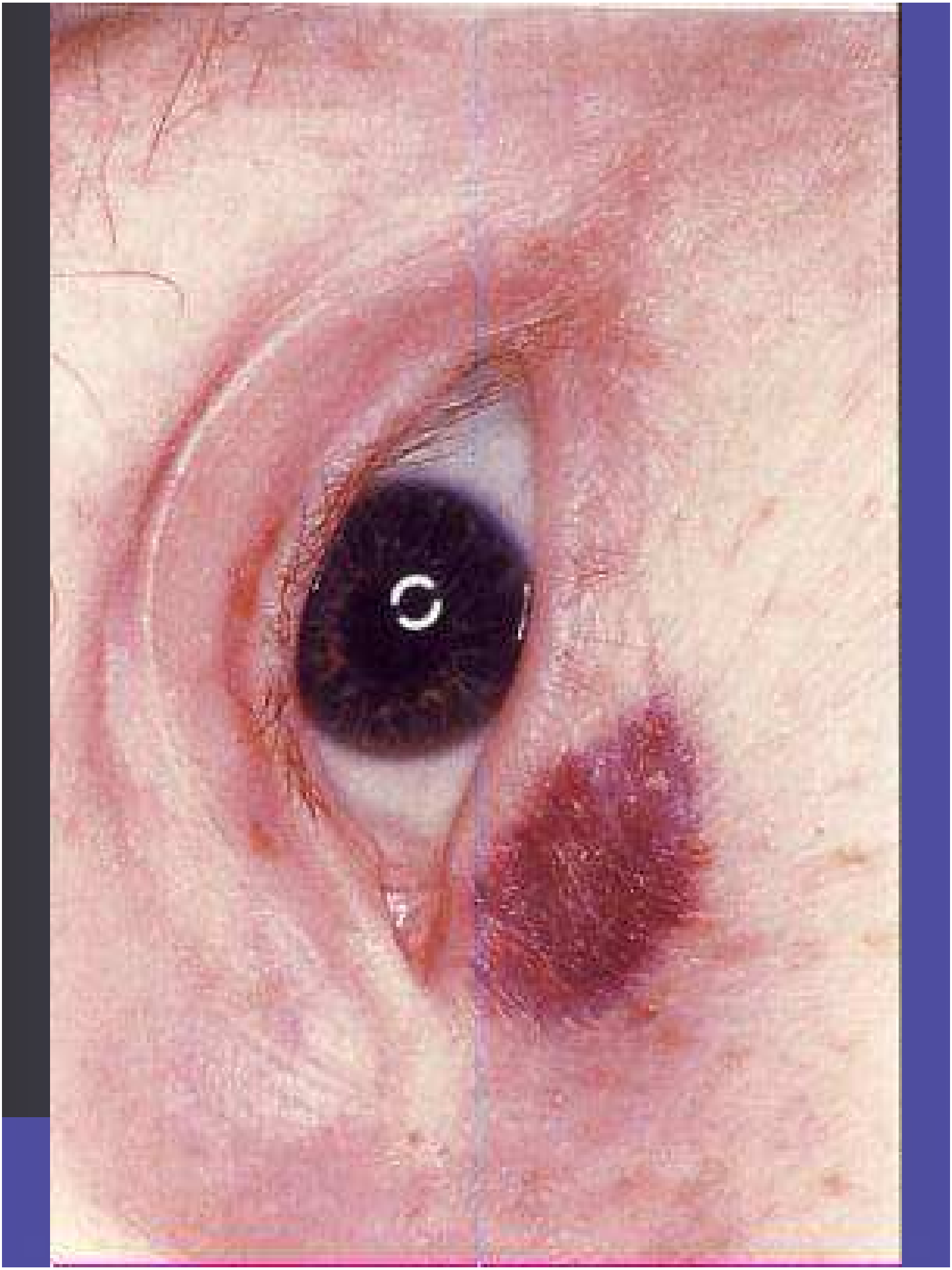


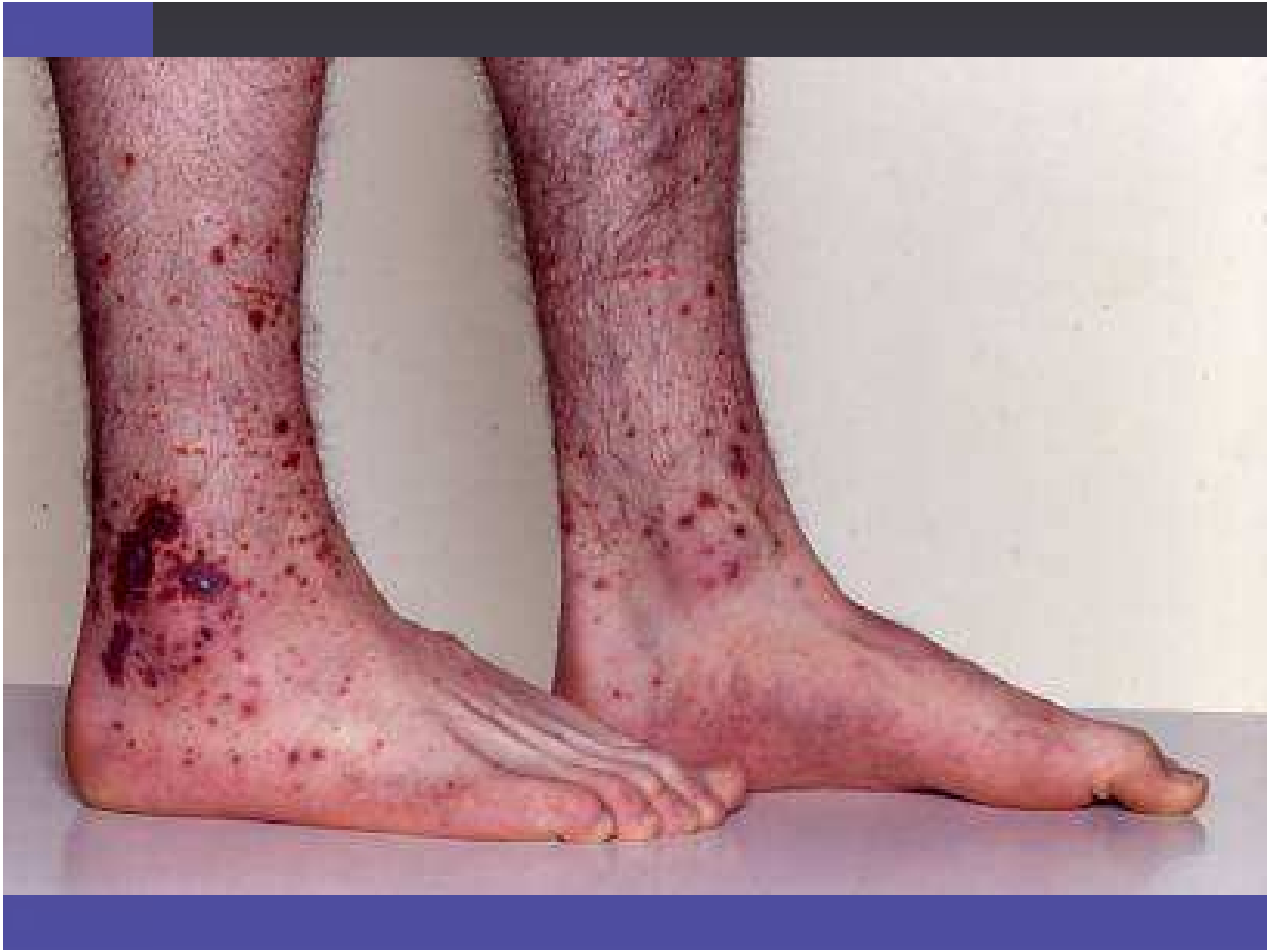
Acquired haemophilia A

- Uncontrollable PPH
- Fetal consequences
- Rapid accurate diagnosis essential
  Referral centre laboratory
- Treatment highly specialised
  rFVIIa, porcine FVIII
  Immunosuppression

Vascular disorders

- Vitamin C deficiency
- Henoch-Schonlein purpura
- Collagen diseases eg Ehlers-Danlos syndrome





Conclusions

- Need for close multidisciplinary team working
  - Clinical and laboratory
- Planning of delivery crucial
- Close and repeated clinical assessment by experienced haemophilia doctor
- Very rapid response to events
- Obstetric units should be closely linked to haemophilia centre