Anesthesia in hemophilia

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Why we should know ??

- In hemophilia
- Life expectancy has increased from 11 years before the 1960s for patients who were severely affected to older than 50-60 years by the early 1980s

- Now near normal !!
- Just 1.2 times more common mortality

The basics

- Vascular
- Endothelium
- Platelets
- Plasma

- Constriction
- Procoagulant
- Adhesion and aggregation
- Fibrin

The three

- The hemostatic response involves three processes characterized as
- (a) primary hemostasis, ***(stage 1)***
- (b) coagulation, (stage 2)
- (c) fibrinolysis. (stage 3)

The process -- stage 1

- Injury → platelet adhere (vWF),
- subsequent platelet activation and aggregation
- (vWf, serotonin, ADP)

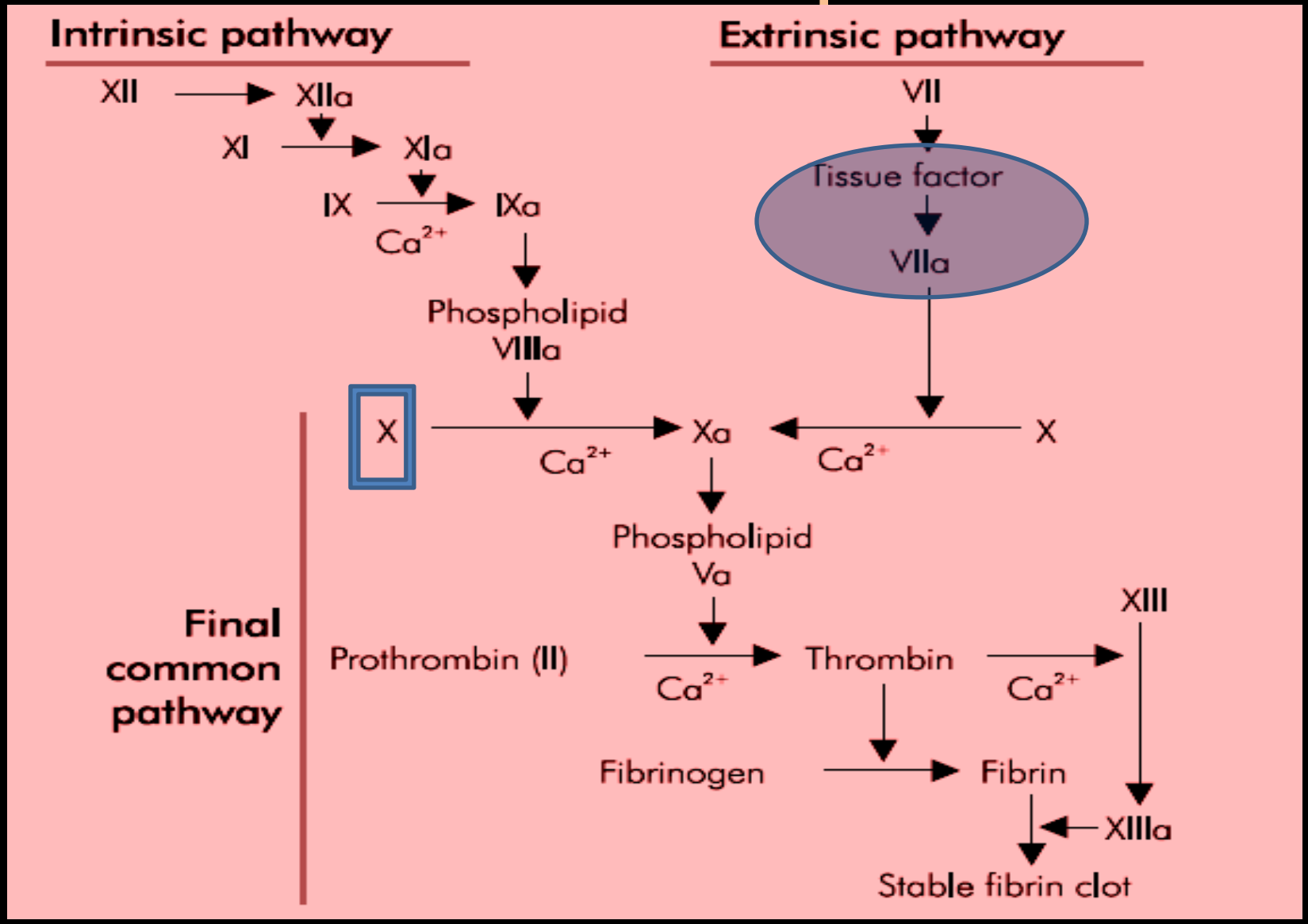
↓

- occlusive platelet thrombus. (plug)

The process – **stage 2**

- Plasma coagulation proteins (*clotting factors*) normally circulate in plasma in their inactive forms
- extrinsic and intrinsic pathways – Active forms
- Endothelial tissue factor + platelet factors

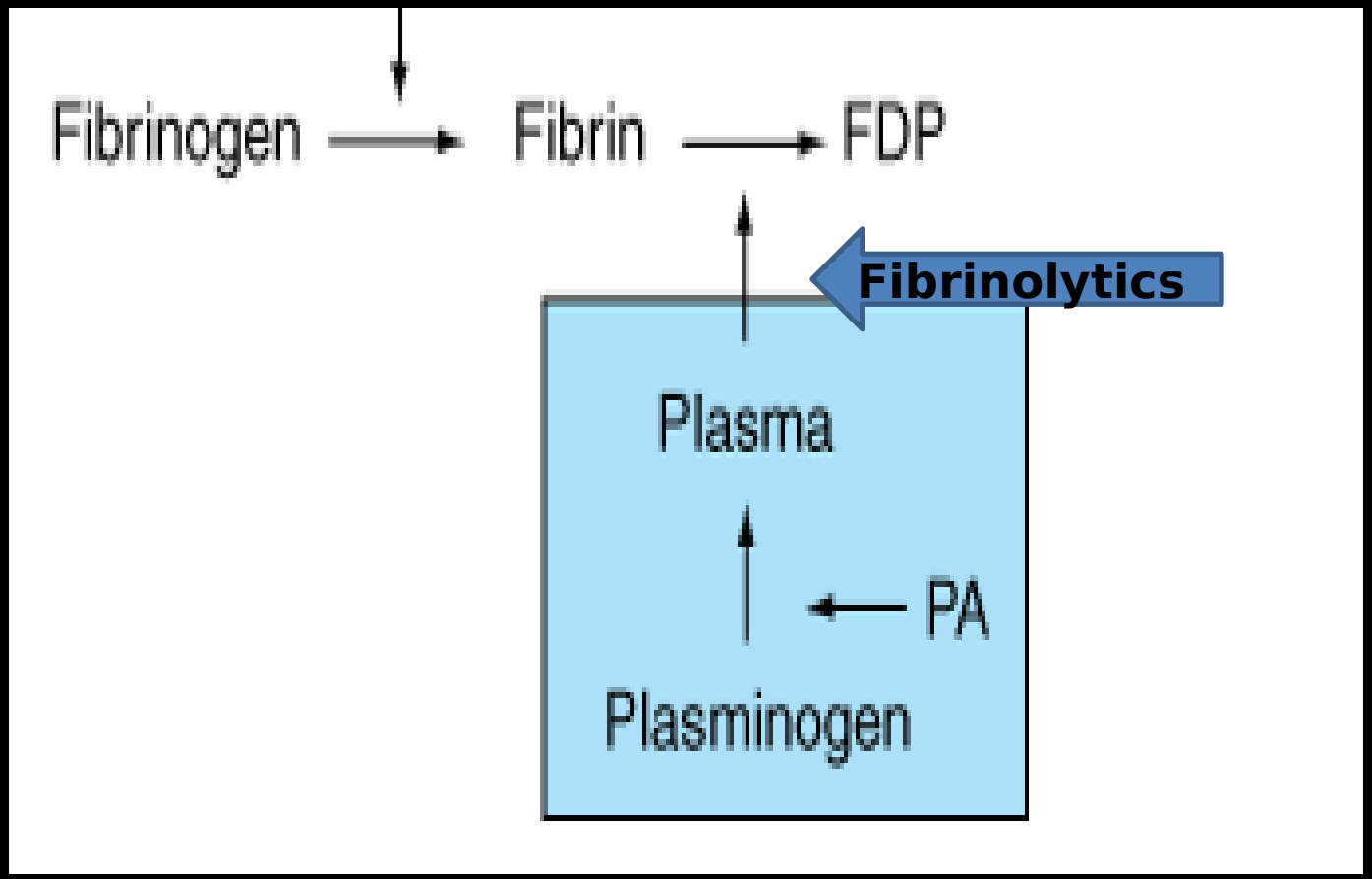
Classic description



Intrinsic extrinsic

- 12, 11,9,8, 7
- ↘ ↙
- 10
- 2
- 1 ← 13

Stage 3


Fibrinogen
Fibrin
FDP
Fibrinolytics
Plasma
PA
Plasminogen

Hemophilia

- A. congenital deficiency of factor VIII
- B - congenital deficiency of factor IX
- C- functional deficiency of factor XI
- Acquired hemophilia – development of factor VIII antibodies

Acquired haemophilia

- development of Factor VIII inhibitors (autoantibodies) in patients without a history of Factor VIII deficiency.
- idiopathic (occurring in people >50 y),
- collagen vascular disease
- peripartum period,
- drug reaction (eg, to penicillin).
- lymphoproliferative malignancies.

The origin of hemophilia

- X-linked trait with variable expression
- The gene for factor VIII is located on the
- long arm of the X chromosome
- 1 in 5000 males
- Females are usually carriers

- They have 2 “X”

Clinical- normal plasma activity – 50 -150 % i.e. 0.5 to 1.5 units / ml

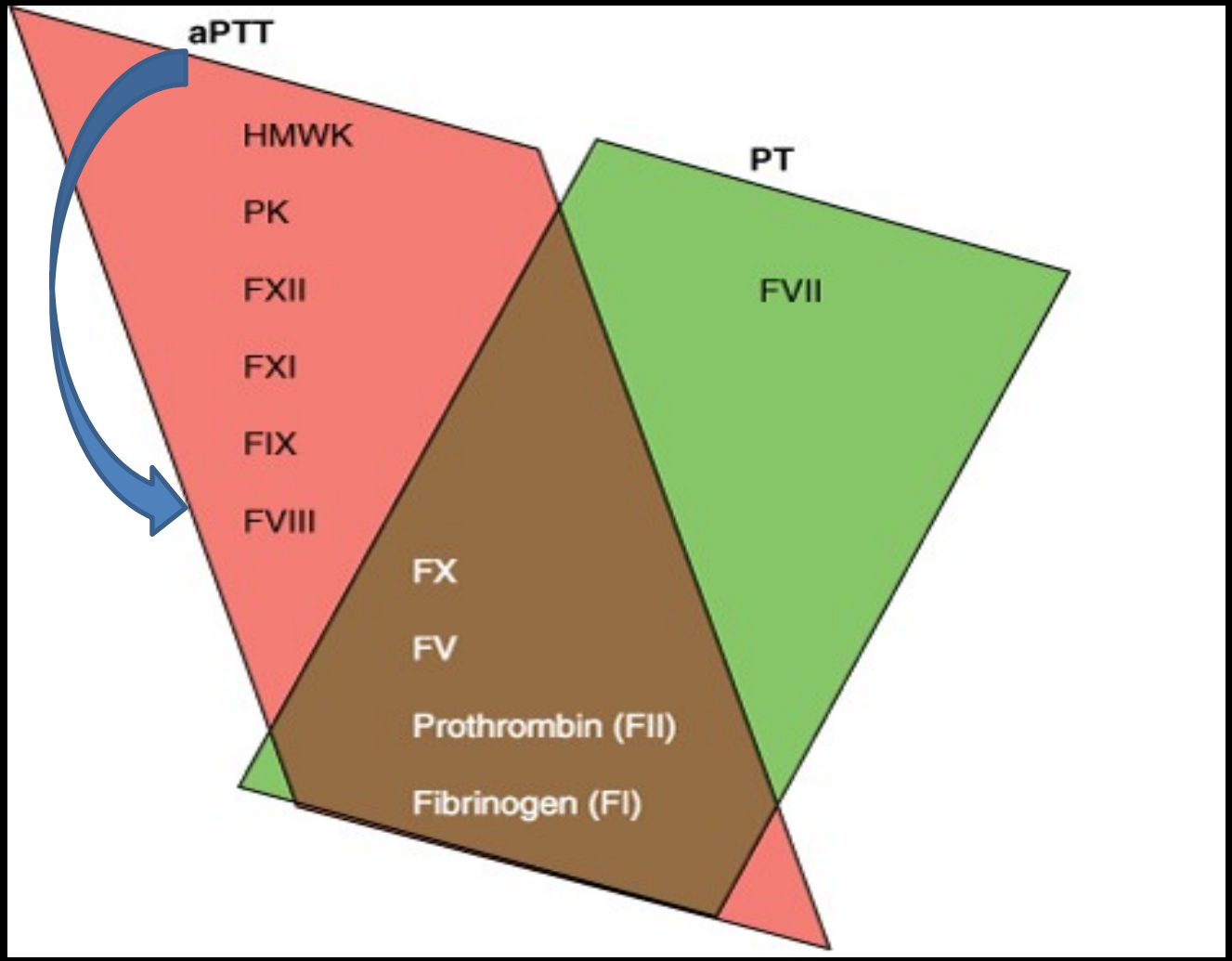
CLINICAL PRESENTATION	FACTOR VIII CONCENTRATION (% of normal)
Spontaneous hemorrhage	1–3
Moderate trauma	4–8
Hemarthrosis and deep skeletal muscle hemorrhage	10–15
Major surgery	>30

It’s a clotting defect

- They don’t bleed more intense
  But they bleed for more time

- Days, weeks – joints , deep tissues ? Brain
- Family history – but in mutations ??
- Normal PT with abnormal apTT

aPTT and PT


aPTT
HMWK
PK
FXII
FXI
FIX
FVIII
PT
FVII
FX
FV
Prothrombin (FII)
Fibrinogen (FI)

Treatment

- Correct the factor deficiency
- Each FVIII unit per kilogram of body weight raises the plasma FVIII level by approximately 2%, with the half-life of 8-12 hours.
- FVIII should be infused by slow IV, at a rate not exceeding 3 ml/minute in adults and 100 units per minute in young children.

Rare side effects

- Nausea,
- Vomiting
- Pyrexia
- Ear infections
- Dizziness

The next choice

- **Cryoprecipitates** are the next choice and provide average 80 units FVIII content in a volume of 30-40 ml.

- **Fresh frozen plasma** may also be used if factor concentrates are unavailable. One ml of FFP contains 1 unit of factor activity.

Factor VIII concentrate:

- purified factor VIII concentrate (dry frozen) is the product of choice for replacement therapy .
- It is preferred because it is stable, easy to handle and store, and contains standardized amounts of coagulating factor, with lower probability of transmitting viral diseases as compared to cryoprecipitate or plasma

Desmopressin

- a synthetic analogue of vasopressin
- boosts plasma levels of FVIII and vWF.
- A single IV infusion of 0.3 mg/kg increases the level of FVIII 3-6 times with peak response in 90 minutes.
- It is ineffective in patients with severe Hemophilia A and is of no value in Hemophilia B.

Desmopressin

- Nasal spray: Weight >50 kg = 300 micg
- (1 spray each nostril)

- Weight <50 kg =150 mic g (1 spray in only 1 nostril)

antifibrinolytics

- Tranexamic acid is an antifibrinolytic agent that promotes clot stability and is useful as adjunctive therapy in Hemophilia.
- Tranexamic acid is given at doses of 25 mg/kg three to four times a day.
- EACA treatment requires a loading dose of 200 mg/kg (maximum of 10 g) followed by 100 mg/kg (maximum 30 g/d) every 6 h.
- No in hematuria because clots obstruct


Inhibitors

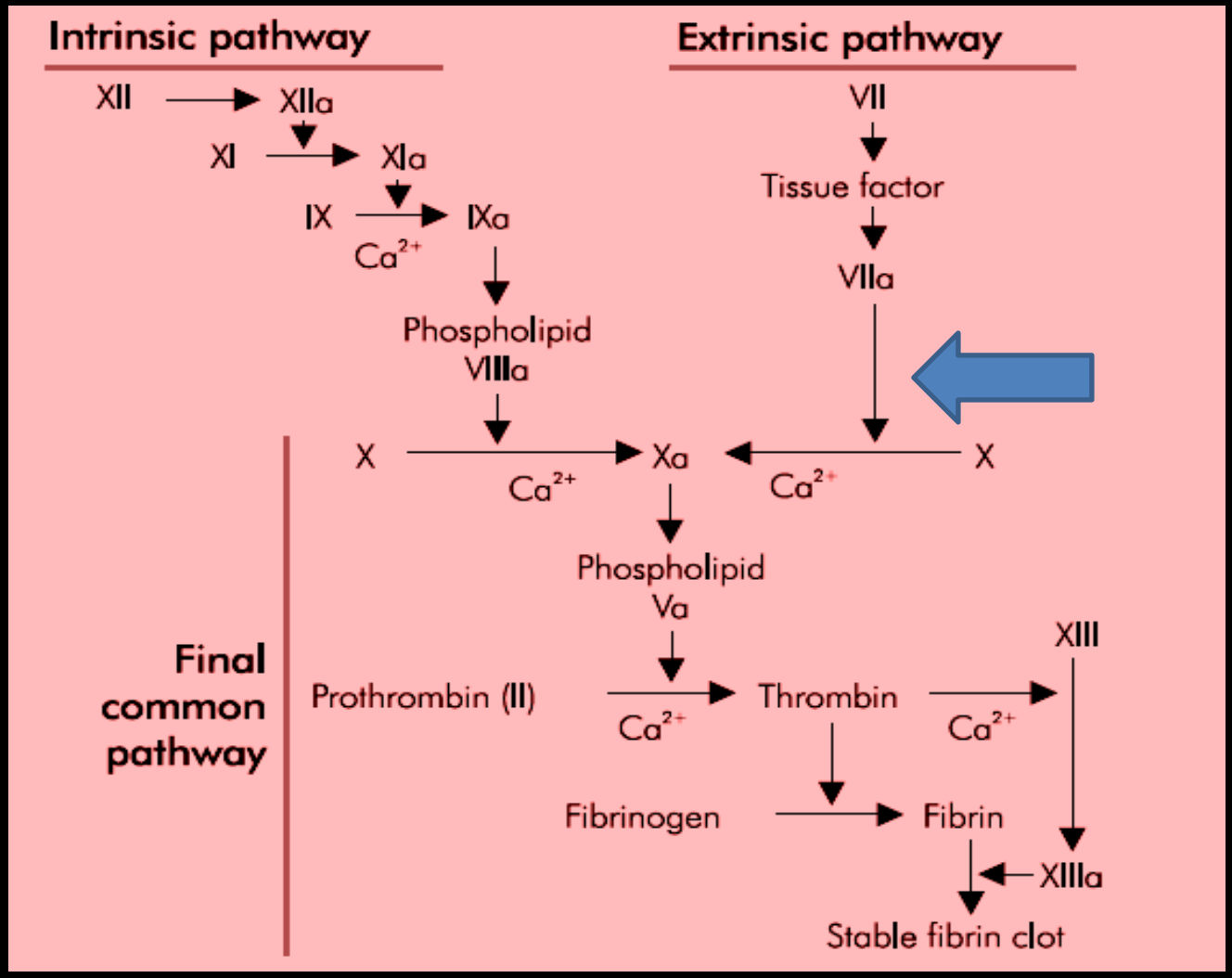
Circulating inhibitors

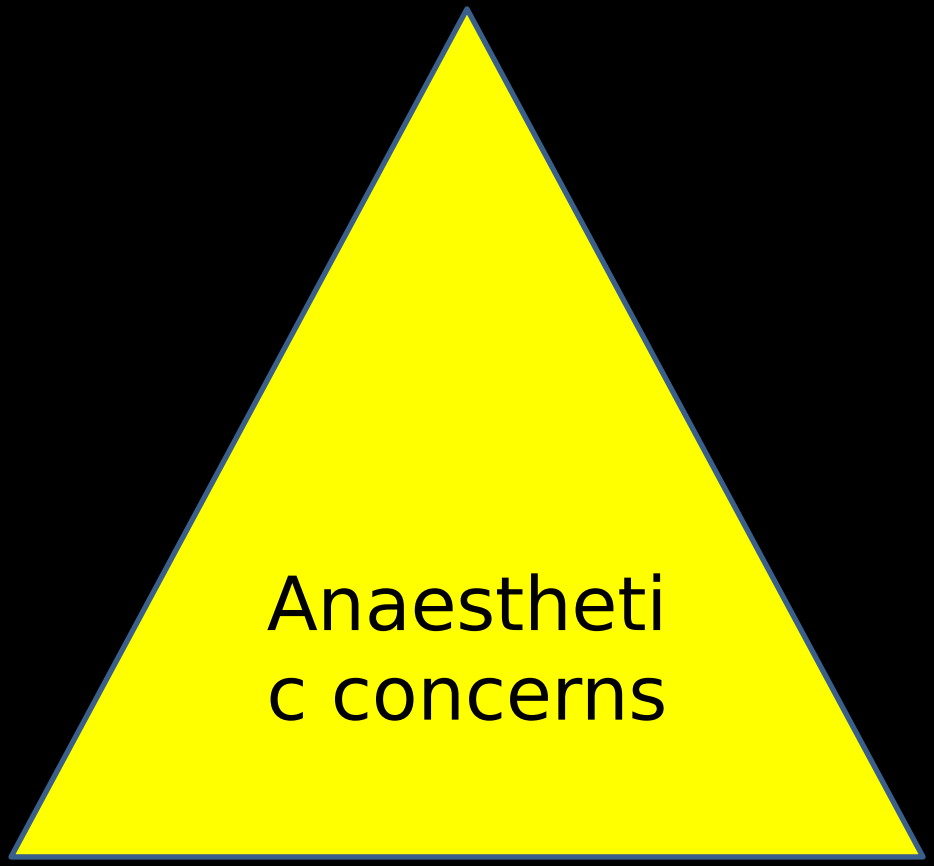
- May develop on chronic therapy of factors
- The “Bethesda unit” of inhibition is defined as the amount of inhibitory activity in 1 mL of plasma that decreases the factor VIII level in 1 mL of normal plasma from 1 to 0.5 units
- More than 10 Bethesda unit – not good
- Novoseven

Novoseven

- NovoSeven is recombinant human coagulation Factor VIIa promotes hemostasis by activating the extrinsic pathway of the coagulation cascade
- **Hemophilia A or B with Inhibitors to Factor VIII or Factor IX**
- **Deficiency of factor VII**
- 35 and 70 µg/kg every 4 hours intravenous bolus administration only
- Acquired hemophilia 90 µg/kg

Novoseven


Intrinsic pathway
Extrinsic pathway
XII
XIIa
XI
XIa
IX
IXa
Ca2+
Phospholipid
VIIIa
VII
Tissue factor
VIIa
X
Xa
Ca2+
X
Ca2+
Phospholipid
Va
Final common pathway
Prothrombin (II)
Ca2+
Thrombin
Ca2+
XIII
Fibrinogen
Fibrin
XIIIa
Stable fibrin clot


Anaestheti
c concerns

Preoperative preparation

- **Admit** even for minor procedures
- Raise factor VIII activity upto 100 %
- Maintain upto 3 days post op
- maintain upto 80 % - 4 – 7 days postop then can decline

Number of units to raise

- N = plasma volume x Kg(weight) x % of activity raise needed
- FVIII dose (IU) = (Target F VIII level – Baseline F F VIII level) x Body Wt. (kg) x 0.5

(100 – 40) x 50 x 0.5 = 60 x 25 = 1500

Desired rise / 2 = 60/2 units / kg

Duration 12 hours only –

Twice a day

Other techniques

- continuous infusion of factor VIII concentrates at a rate of 3 U/ kg/h through a **dedicated line. (80 %)**
- Peak and trough factor VIII levels should be measured to confirm the appropriate amount of factor VIII to be infused and the dosing interval

F IX dose (IU/kg) = (desired rise in FIX IU/dL) ÷ 0.85

Infusion

- Factor VIII concentrates are very stable at room temperature after reconstitution
- By titrating the infusion, the desired factor VIII level can be maintained,
- infusion technique requires close observation,
- less total factor VIII is infused and therapeutic levels are maintained.

Post op

- Therapy must be continued for up to 2 weeks to avoid postoperative bleeding that disrupts wound healing.

  Longer periods of therapy (4 to 6 weeks) may be required in patients who undergo **bone or joint surgery.**

Are we ready

- Major surgery in an adult with an average weight of 70kg, with severe haemophilia A when intermittent therapy is employed will generally require between 50,000 and 80,000 units of factor VIII.

Surgery	No significant resource constraint		Significant resource constraint	
	Desired level (IU/dl)	Duration (days)	Desired level (IU/dl)	Duration (days)
Major				
Preoperative	80-100	-	60-80	-
Postoperative	60-80	1-3	30-40	1-3
	40-60	4-6	20-30	4-6
	30-50	7-14	10-20	7-14
Minor				
Preoperative	50-80	-	40-80	-
Postoperative	30-80	1-5*	20-50	1-5*

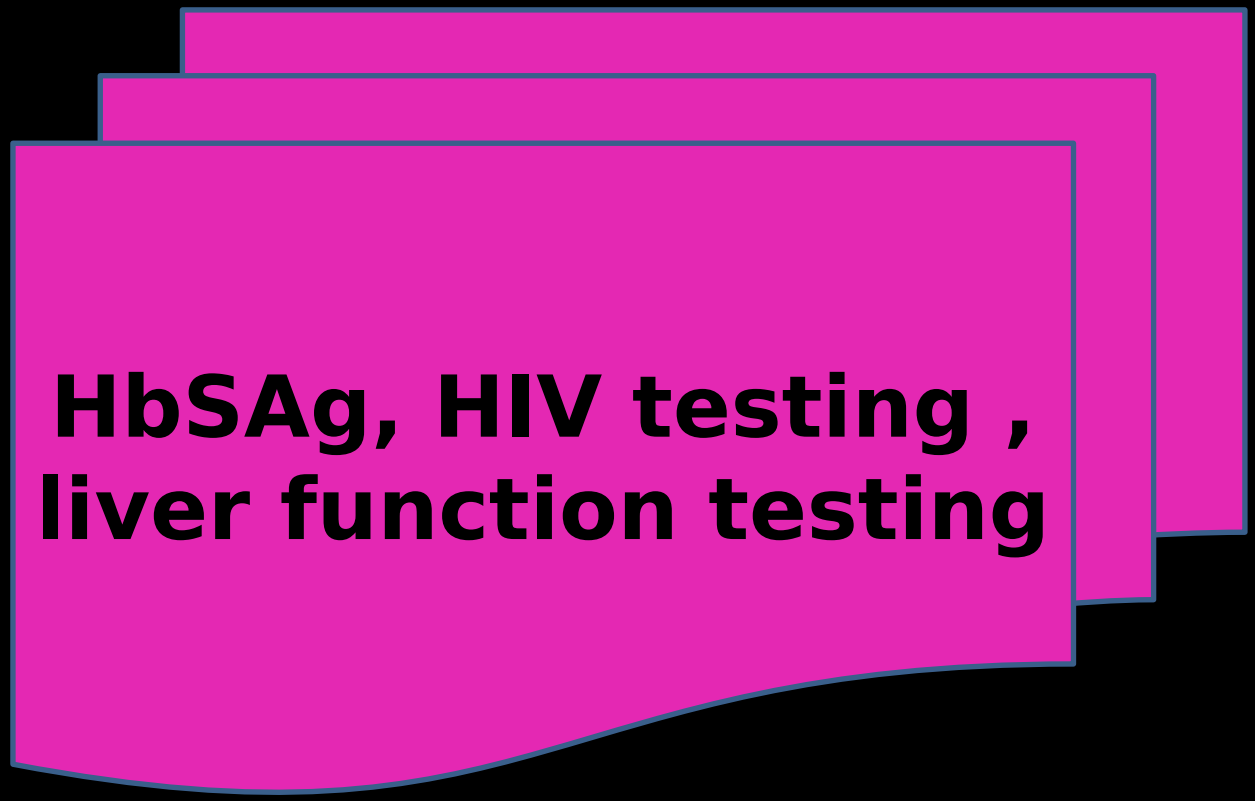
*Depending on the type of procedure

Types of surgeries

- Intracranial bleeds
- Pediatric lip injuries
- Hematomas and pus
- Septic knee
- Orthopedic procedures
- Dental

- Elicit records of previous surgeries and replacements

Preoperative cautions



- **But recombinant technology overcomes**

During preanesthetic evaluation

- status of joints, look for spontaneous hematomas,
- check tracheal intubation conditions and the presence of oral injuries (especially endo and periodontal injuries, which are very common) .
- Know the procedure done
- Hematologist discussion

Other anaesthetic aspects

- No IM premedication
- Vascular access careful
- CV catheters – USG guided

- Positioning: monitoring patients' position on the operating table observing their articular limitations;

GA

- Careful vascular access
- Smooth induction
- No scoline
- Tube greased
- Beware of Ryles tube and temperature monitors
- Hypertension and tachycardia during surgery in Hemophiliacs can lead to increased surgical bleeding.

GA

- Avoid nasal intubation
- If possible airway maneuvers can be avoided – suction !!
- Intubation - the risk of airway bleed remains- smaller tube
- Associated liver illness -- careful
- Careful padding of limbs

Pain relief

No NSAIDs

NO IM injections

Paracetomol OK

PCA narcotics ideal

Discharge !!!

Home infusion of purified factor VIII concentrate has been shown to be safe, efficacious and convenient for postoperative patients and should be used for this patient.

Blocks – ok Yet

- Regional blocks – safely performed if factor VIII levels are corrected.
- Epidural spinal have been performed and reported - uneventful
- Subarachnoid block with smaller gauge needles preferable to epidural but after correction of **Factor VIII and apTT**
- Elective case – consider GA

check post-operative coagulation

- During the post-operative period - obtain assays of plasma levels following FVIII or FIX replacement (peak levels) and also trough levels.
- This may be performed a minimum **of once a day** during the first 2-3 days and less frequently thereafter.
- Removal of sutures, drains and physiotherapy manoeuvres are best carried out at the time of peak levels.

Axillary catheter – OK

- Risk of bleeding in our patient from a CABPB catheter should be no higher than that of a patient without hemophilia provided that **patient's FVIII level was maintained above 80 percent** while the catheter was being placed and then above 30 percent thereafter

Scrupulous surgeon – small bleeds – take care of



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- Management of pregnancy in a patient with severe haemophilia A
- Labour analgesia is possible

Summary

- Types
- Incidence
- Pre op work up and doses
- Other drugs
- Intra op management
- Post op period
- Labour analgesia

Thank you all

