

Evaluation of intracranial bleeds in children with coagulation disorders

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Objective and design

- To evaluate the children having intracranial bleeds with coagulation disorders.
- Retrospective study

Place and duration of study

- Hemophilia Centre Children Hospital
Pakistan Institute of Medical Sciences
Islamabad (January 2005-December
2006)

Materials and Methods

- Total patients registered with Hemophilia Centre were 403.
- Patients presenting with bleeds and managed at the centre over January 2005 till December 2006 were 1980.
- Out of these four cases presented with intracranial bleed. Their detailed history, clinical examination and investigations were recorded.

Case 1- 1st episode

Name	Warid
Age	Two years
Sex	Male
Address	Rawalpindi
DOA	30-07-2007

Known case of FX deficiency registered with Haemophilia treatment centre since August 2006. He presented several times with bleeding episodes, mostly of right knee bleed. Everytime he received FFPs 1 unit/10kg.

Presenting complaints

Headache

1Day

Vomiting

1Day

Fits

1Day

NO H/O fall and NO H/O head
injury

General physical examination

Pulse	100/min
BP	90/60mmHg
Temperature	98F
R/R	20/min
Pallor	+
Jaundice	-
LN	NP

Systemic Examination

CVS

NAD

Resp. S

NAD

GIT

No Visceromegaly

CNS

Neck rigidity+
Reflexes brisk

Laboratory investigations

Blood_CP	Hb	10.4 G/dl
	TLC	$13 \times 10^3 / \mu\text{l}$
	PLT	$373 \times 10^3 / \mu\text{l}$
	MCV	80 fl
	MCH	26 pg
	MCHC	30 g/dl
	RDW	18%

Differential Count:

Neutrophils	60%
Lymphocytes	35%
Monocytes	04%
Eosinophils	01%

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COAGULATION SCREEN

PT (patient) failed to clot

PT (control) 12 secs

PT(patient+control) 15 secs

APTT (Patient) failed to clot

APTT (control) 32 secs

APTT (patient+control) 42 secs

TT(patient) 17 secs

TT (control) 17 secs

Factor XIII

not deficient

Mixing Studies:

APTT

(patient+adsorbed plasma)

124secs

APTT

(patient plasma+aged serum)

40secs

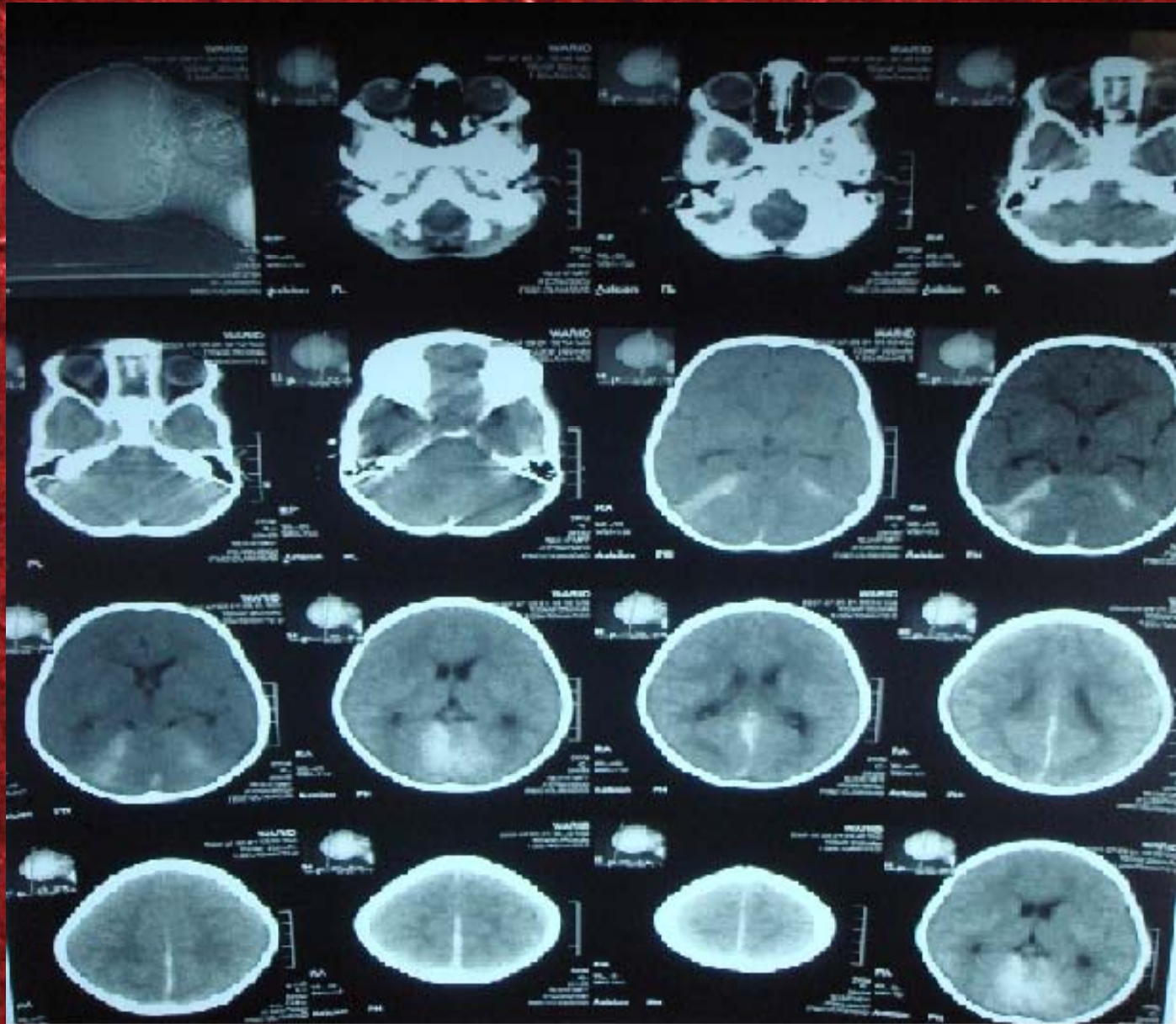
Fibrinogen

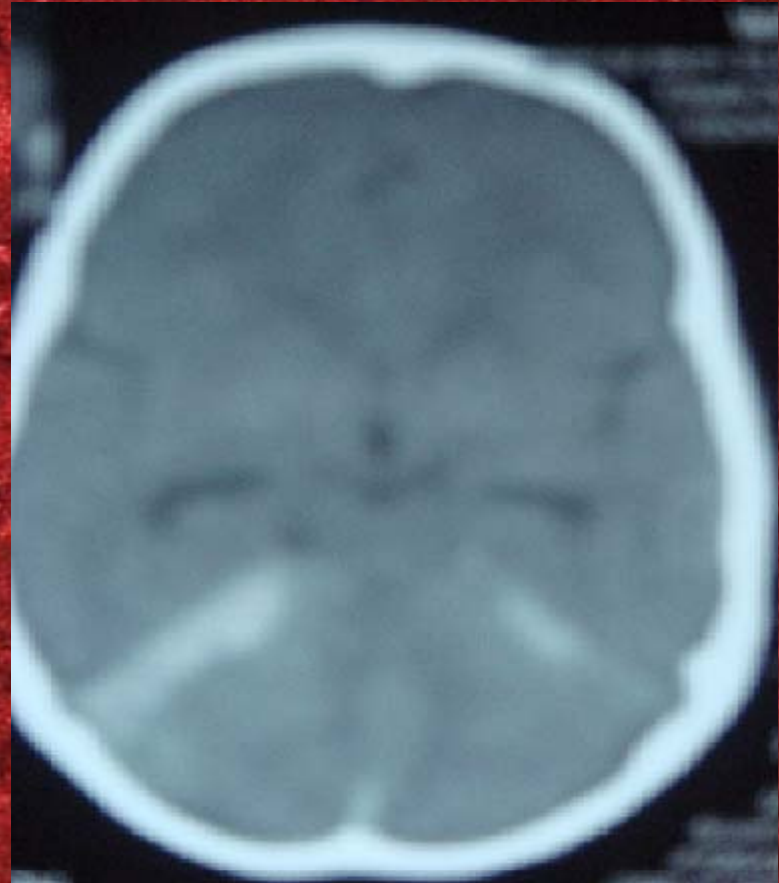
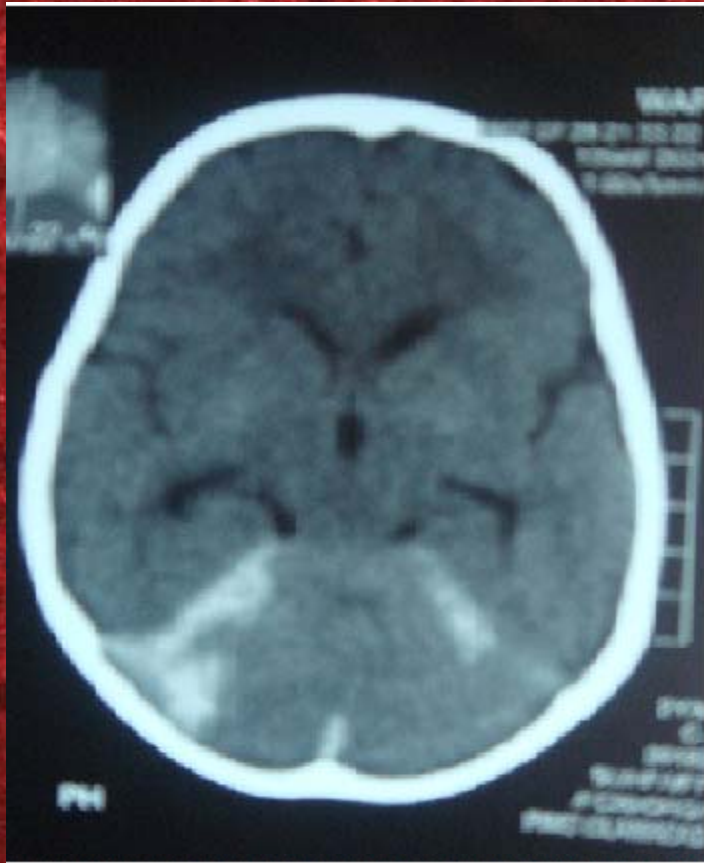
360mg/dl

Opinion: Factor X deficiency detected

Factor X assay

<01%





**Conclusion : subarachnoid
haemorrhage**

Treatment

- FFPs were given daily at a dose of 1unit per 10 kg.
- General condition improved on the 3rd^h post intracranial bleed day .
- FFPs were given for a period of about 17 days till he fully recovered and discharged.

2nd episode

- Date of admission 07-12-2007 in the surgical ward.
- History of fall.
- Presenting complaints were vomiting and drowsiness.

On examination

- Patient was drowsy
- Pulse 82 per min
- Blood pressure 110/60
- Respiratory rate 20/min
- Temperature normal

Treatment

- I/V fluids
- I/V antibiotics
- FFPs were given at a dose 1unit/10kgx10days
- Pre infusion factor activity was 5%
- Post infusion factor activity was 38%
- Patient recovered fully, and was discharged.

Case 2

Name	Ziauddin
Age	1 year
Sex	male
Address	Neelam AJK
Date of admission	18-01-2008

Known Haemophiliac FVIII deficient diagnosed at the age of three months and he was registered with the Haemophilia treatment centre since 09.09.05.

Presenting complaints

Haematoma lower back	1day
Hemiplegia of the right side	1day
Fits	1 day

H/O present illness

There was history of fall.

This haematoma at the lower back was due to the lumbar puncture performed at Muzaffarabad hospital.

General physical examination

Pulse	90/min
BP	90/60mmHg
Temperature	98F
R/R	24/min
Pallor	+
Jaundice	-
LN	NP

Systemic examination

CVS

NAD

Resp S

NAD

GIT

No Visceromegaly

CNS

Neck rigidity++
Reflexes brisk

Blood_CP

Hb	6.4G/dl
TLC	$8.9 \times 10^3 / \mu\text{l}$
PLT	$466 \times 10^3 / \mu\text{l}$
MCV	64.3 fl
MCH	19.9 pg
MCHC	30.9 g/dl
Retic	0.5%

Differential Count:

Neutrophils	40%
Lymphocytes	52%
Monocytes	05%
Eosinophils	03%

Coagulation Screen

Bleeding time	03 mins 15 secs
PT (Patient)	13 secs
PT (control)	12 secs
PT (patient+ control)	12 secs
APTT (Patient)	83 secs
APTT (control)	32 secs
APTT (patient+control)	36 secs

- Factor XIII deficient

not

- **Mixing Studies**

APTT (patient+adsorbed plasma) 42secs

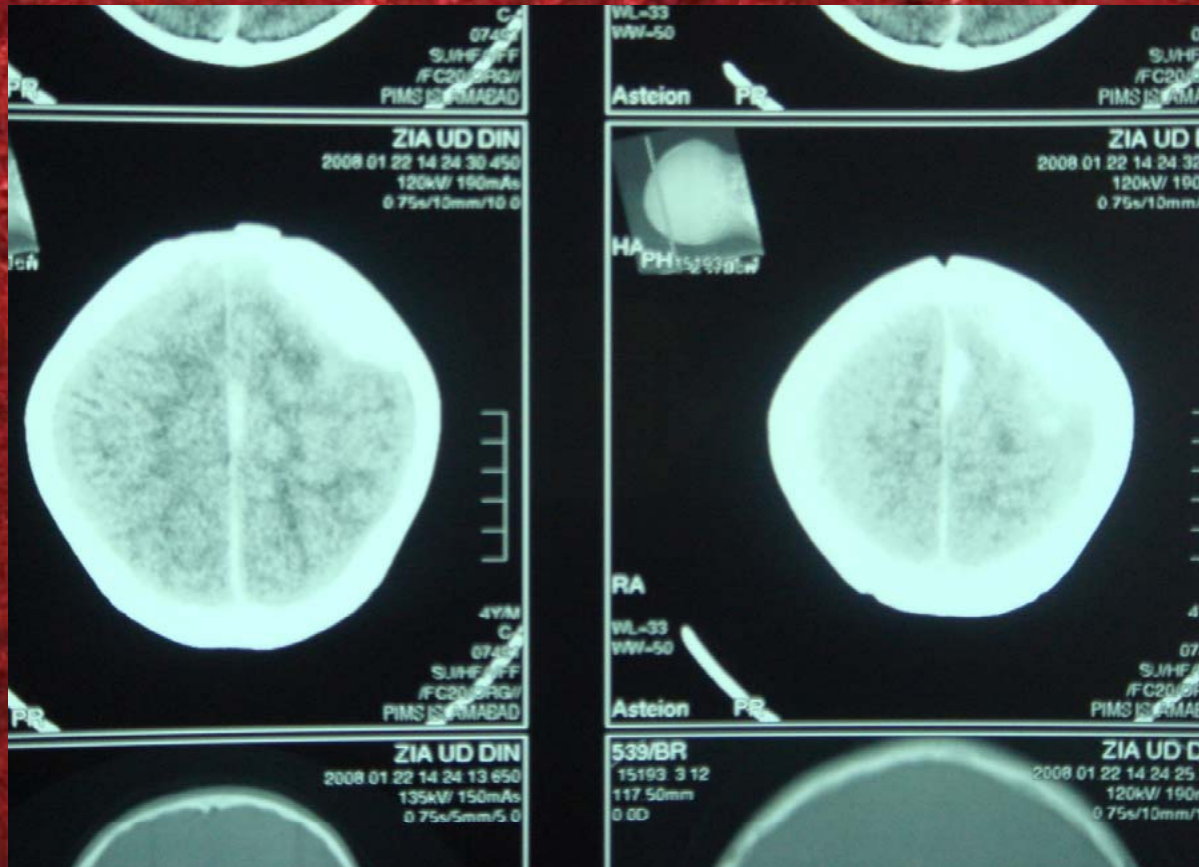
APTT (patient plasma+aged serum) 81secs

Opinion: Factor VIII deficiency detected

- Factor VIII assay

[at the time of registration] 12%

CT SCAN



Treatment

- Injection Factor VIII C 290 units I/V stat followed by 290 units daily for twelve days
- I/V antibiotics.
- This treatment was continued for 14 days and the patient was discharged with full recovery.

Case 3

Name	Abid
Age	eleven years
Sex	Male
Address	AJK
DOA	04-12-2007
	In East Medical Ward

He was a hemophiliac diagnosed at circumcision. The factor level was $< 01\%$, and he was on FVIII concentrate whenever there was a bleeding episode.

Presenting complaints

presented in comatose condition with a history of vomiting.

ON EXAMINATION

- Blood pressure 100/60
- Pulse 70 per min
- Respiratory rate 14/min
- Temperature normal
- No response to any stimulus
- Reflexes were sluggish

Investigations

- Factor VIII assay <01%

CT SCAN





Treatment

- Factor VIII C 12500 u I/V stat
- FFPs 4 units were given
- after 8 hours
- Despite this treatment the patient expired the same day

Case 4

Name	Mohammed Atique
Age	four years
Sex	Male
Address	Attock
DOA	18-05-2007

- Registered with hemophilia treatment centre since 15.05.06. He was receiving FFPs whenever there was a bleeding episode.

Presenting complaints

Vomiting

1 day

Headache

1 day

H/O present illness

History of fall

On examination

Pulse	95/min
BP	85/60mmHg
Temperature	98F
R/R	24/min
Pallor	+
Jaundice	-
LN	NP

Systemic Examination

CNS

Neck rigidity+
Reflexes brisk

Investigation

Blood CP:

Hb	6.1 G/dl
TLC	6800/ μ l
PLT	171 \times 10 ³ / μ l
MCV	80 fl
MCH	26 pg
MCHC	30 g/dl
RDW	18%

Differential Count:

Neutrophils	57%
Lymphocytes	40%
Monocytes	02%
Eosinophils	01%

Coagulation screen

Platelet count 171X10³/μl

Bleeding time 14 mins

PT (Patient) 13 secs

PT (control) 12 secs

APTT (Patient) 70 secs

APTT (control) 32 secs

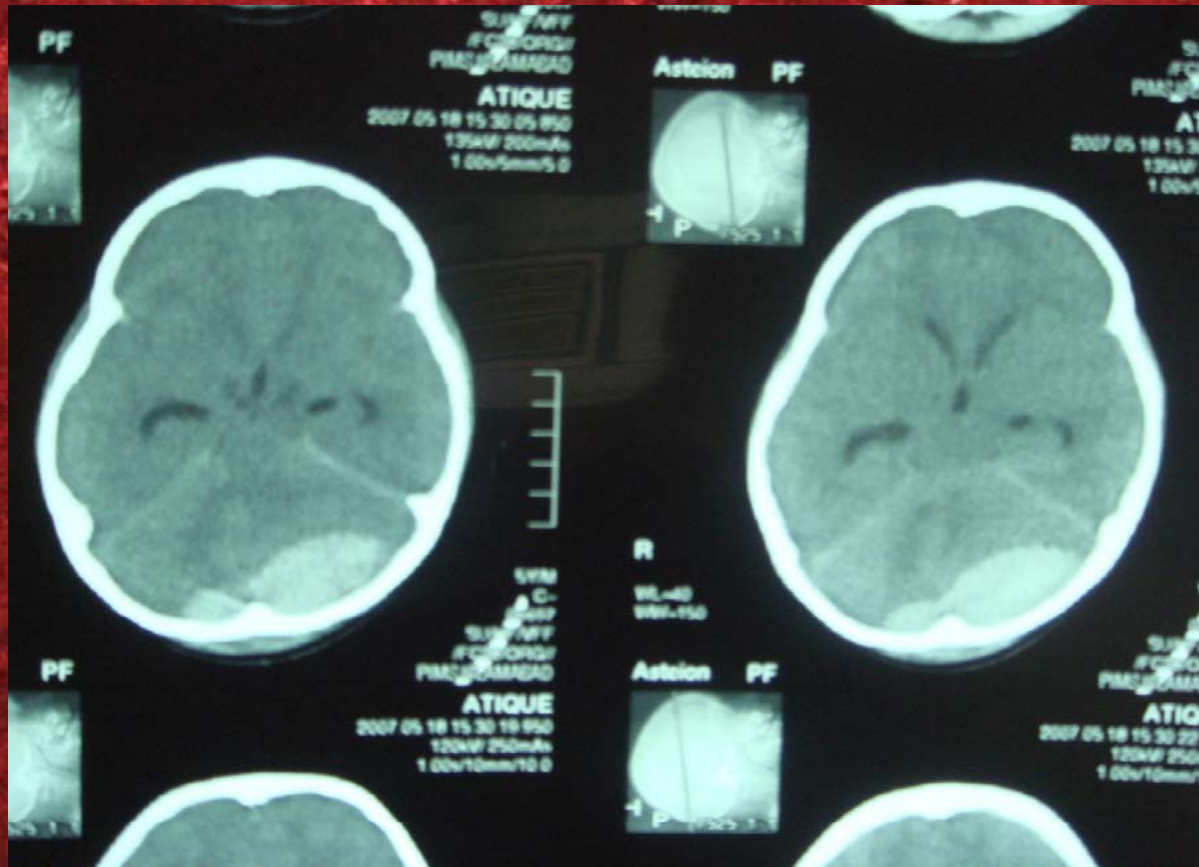
TT 11 secs

Picture suggestive of von Willebrand's disease

Tests to be advised

- Platelet function tests
- Von Willebrand factor antigen levels
- vWF- activity(Ricof)

CT SCAN



Treatment

FFPs

1unit/10kg were
given for 02

weeks

The patient fully recovered and
discharged.

Bleeding complications in coagulation disorders

- CNS bleeding after slight head injury
- Intestinal bleeding might present as intestinal obstruction, haematemesis or melaena
- Sudden oropharangeal bleed might present with respiratory obstruction
- Ilio-psoas bleed might be presented as acute abdomen

PLASMA PREPERATIONS	FACTORS PRESENT
Normal plasma	All factors present
Patients on oral anticoagulant therapy 48-72 hrs	All factors are present except factor VII
Patients on oral anticoagulant therapy after one week	All factors are present except factors II, VII, IX, X

Aged plasma

All factors are present except factors V, VIII C

Adsorbed plasma

All factors are present except factors II, VII, IX, X

Serum

All factors are present except factors I, II, V, VIII C

Transfusion of plasma and platelet concentrates

- Platelet rich plasma
- Platelet concentrate
- Platelet poor plasma that can be separated into
 1. Fresh frozen plasma FFP
 2. Frozen plasma
 3. Cryoprecipitate
 4. Stored plasma

Fresh frozen plasma

- Obtained for single unit of blood
- Rapidly frozen within six hours after donation
- ABO and Rh group specific
- 200ml prepared from 1 unit of blood
- 200ml contained 200 units of each factor
- Must be stored below -30°C
- Shelf life 1 year

Cryoprecipitate

- Plasma component having factor VIII, vWF, fibrinogen, fibronectin and F XIII.
- Obtained from single donation by rapid freezing within 6 hours of collection, subsequent thawing at 4-8 °C and removal of supernatant
- ABO and Rh specific 1 unit is of 20 ml containing 80 i-u of factor VIII
- Shelf life 1 year below -30 °C

Frozen plasma

- Separated from the whole blood within 24 hours
- Contains 50% of the original factor V and VIII
- Shelf life is 1 year below -30°C

Stored plasma

- Separated from the whole blood after 24 hours of storage at 4° C. supernatant plasma is formed after cryoprecipitate production.
- Reduced levels of factor V and VIII in it.
- plasma product do not require cross matching but should be ABO compatible

Coagulation factor concentrate

- Prepared in a freeze dried form
- Given in congenital coagulation deficiencies
- Should not be used for mild acquired deficiency
- Mild factor deficiency should be treated with frozen plasma or FFP

Factor VIII concentrate

- Freeze dried (lyophilized) preparation obtained by large pool of FFPs
- 1 vial contains 250, 500, 1000 i-u
- Constituents
 1. Factor VIII, vWF
 2. Fibrinogen
 3. Anti A anti B antibody
 4. Heparin
 5. Traces of other plasma proteins and dextrose
- Shelf life 2years at 6-8°C

Indications of factor VIII

1. Treatment and prevention of bleeding in patients with Haemophilia A
2. Treatment of bleeding with severe vW disease
3. Treatment of bleeding in patients with factor VIII C antibodies
4. Low responders can be treated with high doses of factor VIII concentrates

Discussions

1. Treatment of suspected intracranial hemorrhage in Haemophiliacs should include prompt replacement therapy and admission to bring the factor level to 80%.
2. Lumbar puncture in Haemophiliacs is contraindicated .
3. Patient should be admitted, investigated and kept under observation. If LP is required it should only be done with replacement therapy.

4. Intracranial Haemorrhage is the most common cause of morbidity and mortality in Haemophilic patients. Despite the treatment mortality rate remained 8.6%. (*Antunes SV, Vicari P, Cavalheiro S, Bordin JO. Haemophilia. 2003 Sep;9(5):573-7.*)
5. From 1995-2004 out of 600 registered patients 37 (6%) were presented with intracranial bleeds. (*Ghosh K, Nair AP, Jijina F, Madkaikar M, Shetty S, Mohanty D. Haemophilia. 2005 Sep;11(5):459-62*)

6. Over 9 years period (1996 to 2004) 43 patients with haemophilia presented 73 times with Intracranial haemorrhage. Intracranial haemorrhage confirmed in 16 %

(Traivaree C, Blanchette V, Armsrtong D, Floros G, Stain AM, Carcao MD Haemophilia. 2007 Sept;13(5); 552-9)

7. Overall incidence of Intracranial haemorrhage has been reported to range from 2.2% to 7.5% in patients with haemophilia. 45 Intracranial haemorrhagic episodes in 35 (8.7%) patients. Mortality 8.6%
*(Antuninus SV, Vicari P, Canalheirio S, Bordin Jo
Haemophilia 2003 Sept; 9(5) ;573-7)*

8. Intracerebral haemorrhage is known to be severe although uncommon complication of Haemophilia. 123 episodes recorded in 106 patients (67.2%) were post traumatic. Overall mortality 21.9%. Morbidity 60% with long term sequelae.

(Stieltjes N, Calvez T, Torchet ME, Fressinaud E Haemophilia 2005 Sept;11(5) 452-8)

THANK YOU