



Clinical Management of Hemophilia in Developing Countries

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Disclosures for:

CONFLICT

DISCLOSURE — IF CONFLICT OF INTEREST EXISTS

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Hemophilia: Not Uncommonly Found



- Incidence 1: 10,000 population
- Estimated 420,000 patients with hemophilia globally
- 180,000 patients are diagnosed
- Only 50% of all diagnosed patients receiving replacement therapy of factor concentrate



Hemophilia: Not Uncommonly Found

- X-linked recessive inheritance, found in males
- Lack of factor VIII or IX resulting in frequent bleeding at the muscles and joints
- In cases of inadequate replacement therapy, patients often die during childhood period. They cannot reach the adulthood.





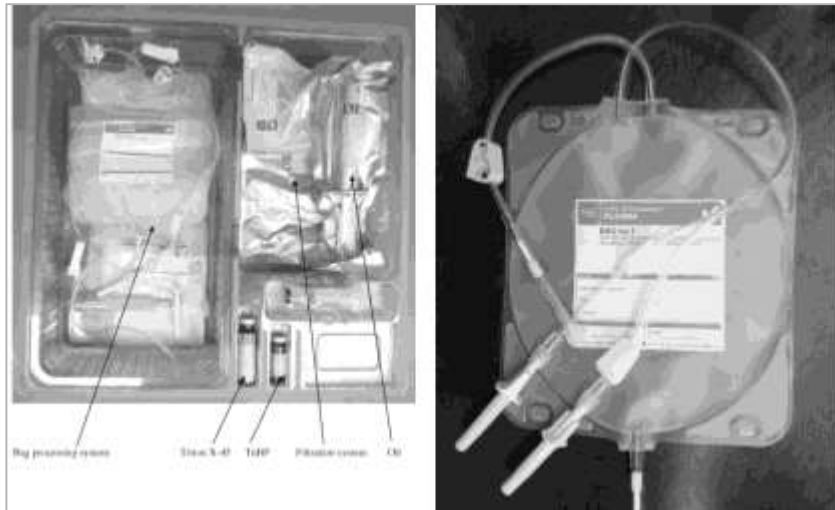
Replacement Therapy



FFP cryoppt
Fresh frozen plasma, cryoprecipitate



Heat-treated lyophilized cryoprecipitate



Solvent-detergent treated cryoprecipitate



Factor concentrate



Management of Hemophilia in Developing Countries

- **Poor awareness**
- **Inadequate diagnostic facilities**
- **Scarce factor concentrates for therapy**



- **Self-reliance and positive attitude**
- **Modified strategy of 'lower-cost treatment' and 'low-tech' intervention**



Management of Hemophilia in Developing Countries

- It is difficult to persuade government to use resources for hemophilia. Advocacy based on humanity, solidarity or emotion is not sufficient
- There is a real need to demonstrate that the resources utilized are justified and the treatment regimens are working





Laboratory Diagnosis of Hemophilia A & B

- Prolonged APTT
- Low level of FVIII:C or FIX:C
- Bedside diagnostic kit
 - First version published in *Haemophilia* 2009;15:361-364.
 - Second version published in *Haemophilia* 2013;19:e48-e49.



WB



WB
+FVIII



WB
+FIX



Important Issues

- **Provide knowledge to patients and parents**
- **Effective bleeding prevention through daily life-style should be emphasized**
- **Although replacement therapy is often not available, simple and effective intervention with ‘RICE’ can lessen the pain of hemophilic children who have bleeding into the muscles and joints**



First Aid Management for Bleeding Episode

R = Rest

I = Ice

C = Compression

E = Elevation





Principle of Treatment

- **Prevention of bleeding**
 - **Avoid trauma, contact sport**
- **Replacement therapy**
- **Comprehensive care**
 - **Rehabilitation**
 - **Dental care**
 - **Immunization**
 - **Infectious & inhibitor screening**
 - **Genetic counseling**





Healthy Diet

- **Healthy diet is important, not to gain too much weight that will burden the joint function and create difficulty in venipuncture**





Replacement Therapy

- **Episodic bleeding treated in the hospital**
- **Early bleeding treated at home, nearby health stations or hospitals**
- **Prophylactic treatment**



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Episodic Treatment

Hemophilia without inhibitor

- **Using lower dose compared to standard regimen based on guideline of World Federation of Hemophilia (WFH)**
- Replacement therapy was initiated when the patients were hospitalized
- **Requiring a larger amount of blood components compared to early treatment**



Episodic Treatment

Hemophilia without inhibitor

- **In cases of emergency surgeries or serious bleeding, risk to volume over load if only FFP were used as replacement therapy**
- **Risk to recurrent bleeding complication if the raised levels of factor VIII and factor IX were lower than standard levels**



Treatment Guideline

Type of bleeding	Level of factor (%)	
	Initial	Maintenance
1. Bleeding at muscle, suture wound, dental procedure*	20-30	–
2. Deep hematoma, hemarthrosis, large wound	40-60	20-30 (3-7 days)
3. Bleeding in vital organs, CNS, GI, ileopsoas muscle, and general surgery e.g. appendectomy	80-100	40-50 (1 week)
4. Major surgery of musculoskeletal, brain surgery	80-100	40-50 (1-3 weeks)

***In case of using fibrin splint, replacement therapy may not be needed**



Episodic Treatment

Hemophilia with inhibitor

- **Bypassing agents of activated prothrombin complex concentrate (APCC) and recombinant activated factor VII (rFVIIa) are more expensive compared to factor VIII and IX concentrates**
- **Using lower dose and few doses of bypassing agents**
- **Risk to more serious bleeding complications**
- **Predisposing patients to more morbidity and mortality**
- **Causing higher treatment cost**



Replacement Therapy

- **Episodic bleeding treated in the hospital**
- **Early bleeding treated at home, nearby health stations or hospitals**
- **Prophylactic treatment**

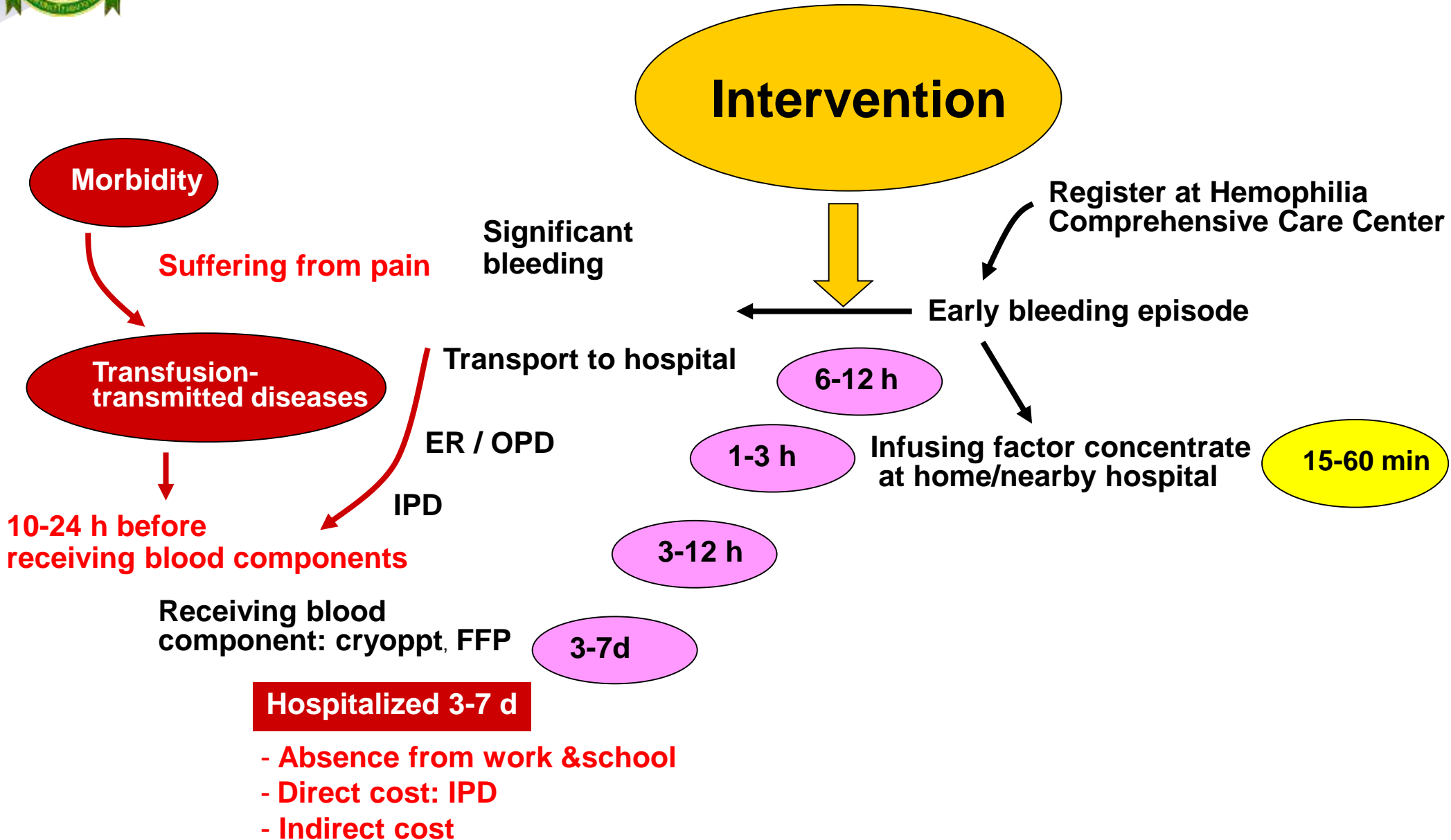


Early Treatment

- **At the first sign of tingling sensation associated with early bleeding into muscles or joints**
- **Immediate after trauma**
- **When treatment is given early, less blood product was used and less further bleeding occurs compared to delayed treatment**



Process Mapping of Treating Bleeding Episode





Exercise to Have Prominent Vein





Patients and Parents

- **Exercise to have prominent vein**
- **Select the venipuncture site and remove the needle while hospitalized**
- **Practice venipuncture on a model and real vein**



Simple Tool for Practicing Venipuncture





Practice Venipuncture in the Hospital





Case Study from Ramathibodi Hospital

- Parents provide proper care to prevent bleeding episodes
- Provide early bleeding treatment at home, nearby health stations or hospitals

1-10 years 250 units every 7 days

11-15 years 500 units every 10 days

16-20 years 500 units every 15 days

- Hospitalization

1-15 years 3 hospitalizations per year

16-20 years 2 hospitalizations per year



Benefit of Early Treatment among Thai Hemophilia

	First decade 1971-1980	Second decade 1981-1990	Third decade 1991-2000
• Number of patients	47	58	59
• Number of patients receiving home treatment	15 (31.9%)	30 (51.7%)	40 (67.8%)
• Number of patients with unaided proper walking	27 (62.8%)	43 (75.4%)	49 (84.5%)
• Proportion of death	14 (29.8%)	8 (13.8%)	3 (5.1%)

Chuansumrit A, et al. Haemophilia 2004;10:542-9.



I. Evaluation Before and After Receiving Factor Concentrate for Treating Early Bleeding in 2007

	Before	After
• Total episode of hospitalization	681	445*
• Episode of hospitalization/case	2.7 ± 3.1	1.8 ± 2.4*
• Days of total hospitalization	3230	1724*
• Days of hospitalization/case	12.8 ± 14.3	6.8 ± 10.7*
• Days of hospitalization/bleed	4.7	3.9*

* $P < 0.001$

Sooksriwong C, et al. Haemophilia 2012;18:e347-e363.



II. Evaluation Before and After Receiving Factor Concentrate for Treating Early Bleeding in 2012

Severity	Policy	Life time cost of treatment (THB)	QALY	Cost per QALY	ICER
Mild	No home base care	4,998,017	23.29	214,595	
	Home base care	5,225,394	26.11	200,103	80,542
Moderate	No home base care	13,659,490	16.47	829,504	
	Home base care	11,198,618	22.44	499,157	Cost saving
Severe	No home base care	25,908,099	12.21	2,122,085	
	Home base care	20,189,367	20.61	979,557	Cost saving

Pattanaprateep O, et al. VIHRI 2014;3C:37-38.



Replacement Therapy

- **Episodic bleeding treated in the hospital**
- **Early bleeding treated at home, nearby health stations or hospitals**
- **Prophylactic treatment**
 - **single dose prophylaxis**
 - **secondary prophylaxis for 1-3 months**
 - **long term prophylaxis**



Prophylactic Treatment

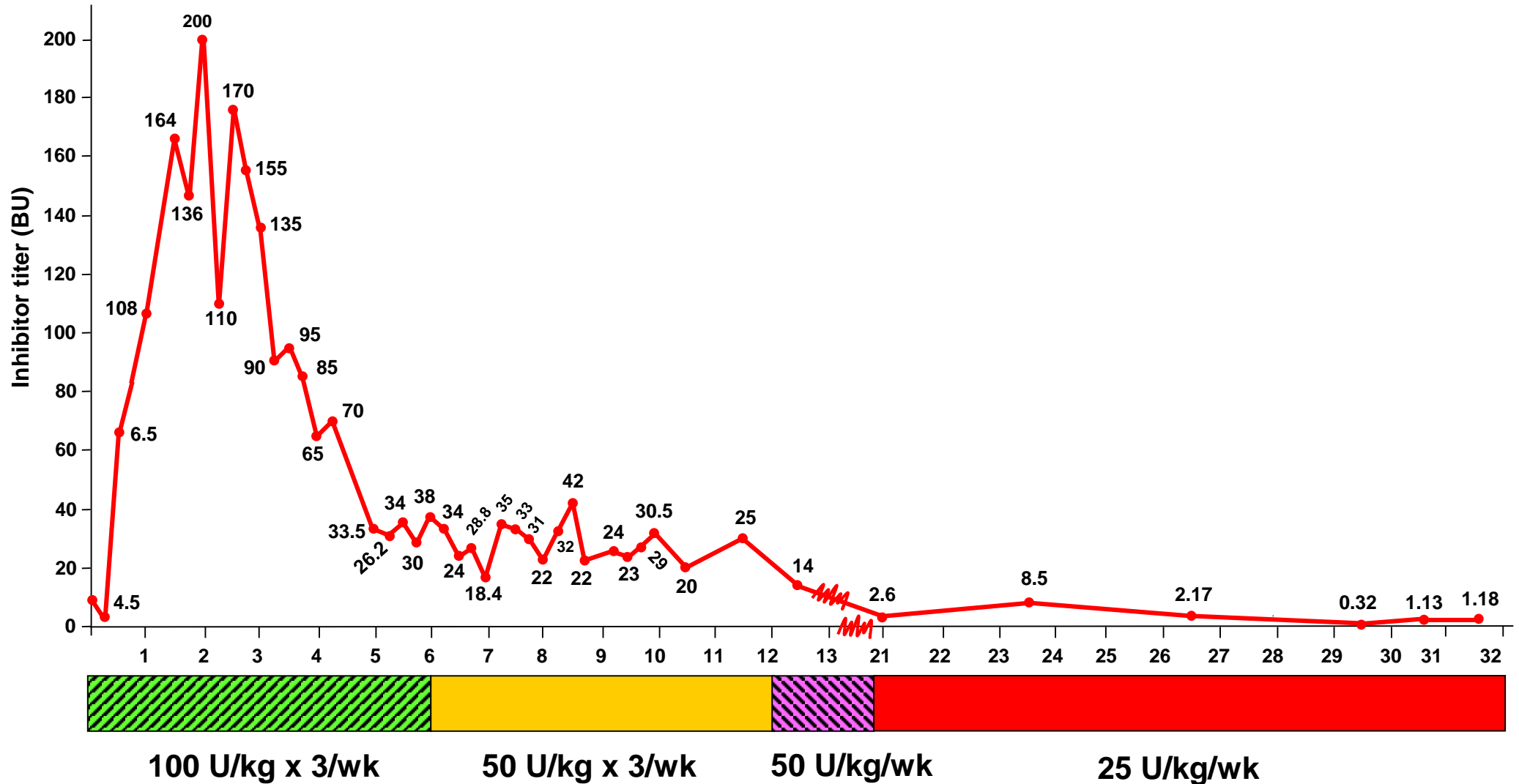
- Standard dose of prophylaxis 25-40 units/kg three times per week for hemophilia A and twice a week for hemophilia B
- Escalated regimen of 50 units/kg once a week, 30 units/kg twice a week and 25 units/kg three times per week
- Low dose prophylaxis of 8-10 units/kg twice a week* or daily 5 units/kg

**Chuansumrit A, et al. Southeast Asian J Trop Med Public Health 1995;26(2):243-246.*





Inhibitor to Factor VIII Clotting Activity



**Thank you
for your attention**

