evropský sociální fond v ČR
EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
UNIVERSITAS MASARYKIANA BRUNENSIS
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Substituční léčba von Willebrandovy choroby různými plazmatickými koncentráty von Willebrandova faktoru

P Smejkal
OKH FN Brno

Více než 30 let neléčitelná choroba

- objevena v dubnu 1924 E. A. von Willebrandem
- publikována 1926
- léčba frakcí I-0 M. Blombäck a I. M. Nilsson 1956

Cohn Fraction from fresh plasma

Extraction with mixture of

glycine 1M
ionic str. 0.3
ethanol 6.5%
pH 6.8

Temp -3%

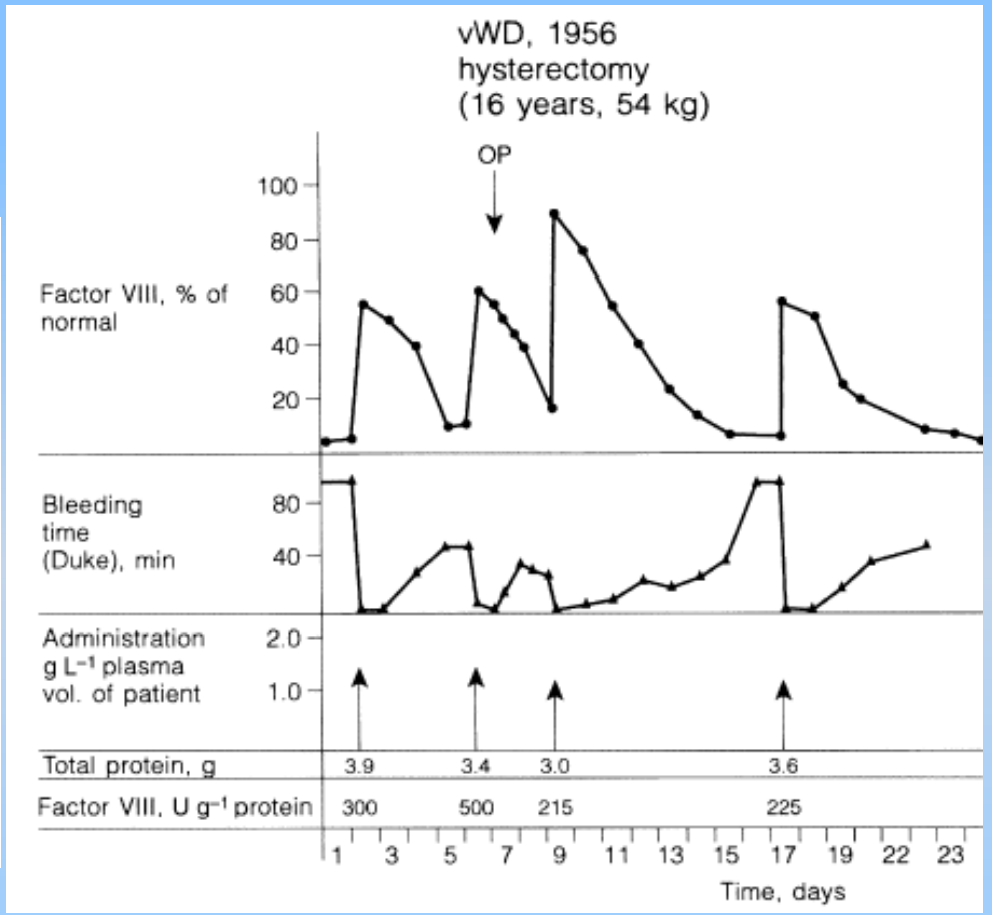
Extract 1 discarded

Extract 2 discarded

I-0 precipitate

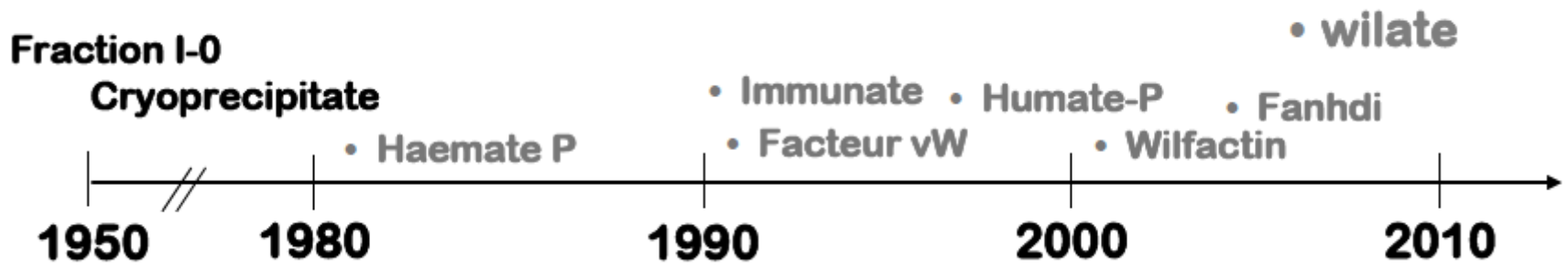
Fibrinogen (yield 96%)
(coagulability 88%)
Factor VIII (yield about 100%)
Bleeding time correcting factor (100%?)

FVIIIR:Ag = VWF:Ag



*Cornu P. Rev Franc Etudes Clin Biol 1960; 5: 614-20, *Blombäck M. Haemophilia 2012; 18: 3-6.

Plazmatické koncentráty VWF v léčbě VWCH
(od roku 1982)



	1980ies	1990ies	2000ies
1st indication	Haemophilia A	Haemophilia A / VWD	VWD / Haemophilia A
Purity [FVIII / total protein]	Intermediate 5 IU/mg	Intermediate 5-30 IU/mg	High >50 IU/mg
Albumin added as stabilizer	Yes	Yes	No
Virus inactivation	Single	Double (+)	Double

**Federici AB. Haemophilia 2006;12 (Suppl. 3):152-8.*

Pharmacokinetics of VWF/FVIII concentrates is a very intricate matter

M. MORFINI
Agency for Haemophilia, Department of Emergency & Reception, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy

The heterogeneity of patients: only type 3 or severe type 1 should be considered in the conduction of single dose PK studies as types 2A or 2M behave differently. Only a few studies have been conducted in type 3 VWD homogeneous cohorts [2,3].

IPC (higher VWF:RCo/FVIII ratio) is able to achieve a lower FVIII concentration than HPC (lower VWF:RCo/FVIII ratio) if the loading and maintenance doses have been tailored according to VWF:RCo content of the

When the FVIII Clearance was evaluated according to the FVIII dose administered, the HPC showed a faster Clearance, about the double that of IPC. This finding

Furthermore, the decay of VWF:RCo of all concentrates is always faster than that of VWF:Ag, indicating a more rapid decrease of the functional properties of the protein

FVIII:C - plateau fáze 12 - 24 hod po aplikaci

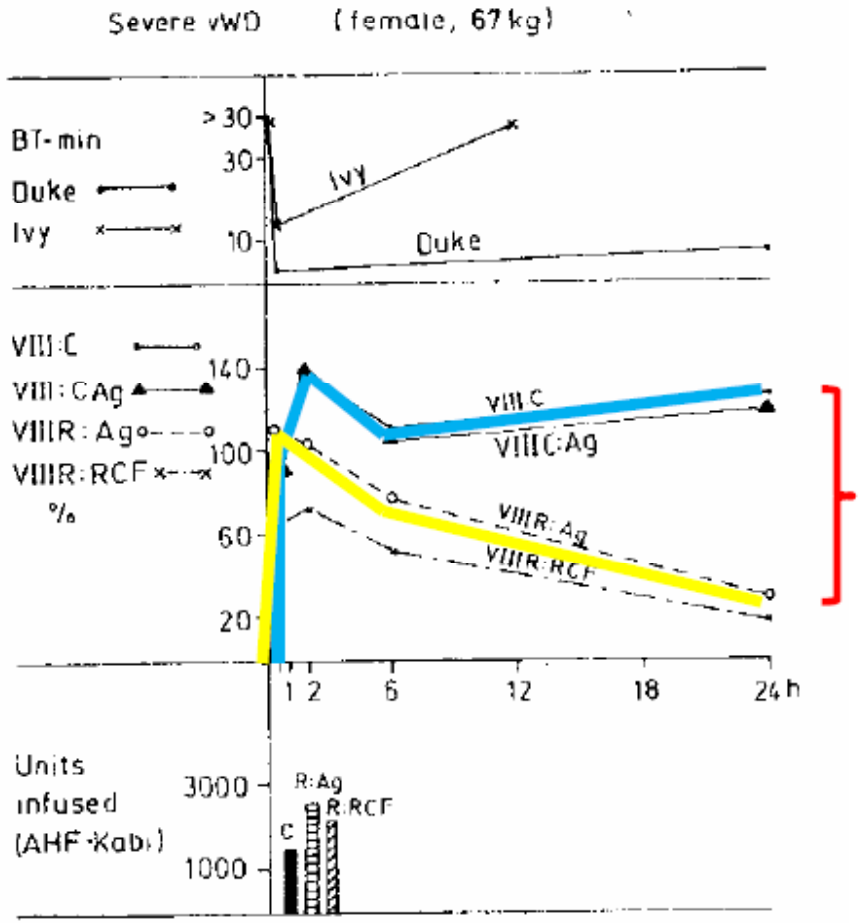


Figure 2. VIII:C, VIII:CAg, VIIIR:Ag, VIII ristocetin cofactor activity (VIIIR:RCF) and Duke and Ivy bleeding time in a patient with severe recessive von Willebrand's disease after infusion of human fraction I-0 (AHF-Kabi).

Nilsson IM. Scand J Haematol 1984;Suppl 40;33:21-43

Porovnání v ČR k léčbě VWCH doporučených koncentrátů FVIII / VWF

preparát	VWF:RCo / FVIII	Recovery / IU / kg		t1/2 (hod.)	FVIII IU / 1 mg	VWF: Rco IU / 1 mg
		Dávkování	Farmakokinetika			
Haemate P®	2,4	2%	1,9%	7	2 - 6	3 - 17
Fanhdi®	1,2	2%	1,9%	14	2,5 - 10	3 - 12
Wilate®	0,9	1,5 - 2%	1,5%	18 - 34	≥ 60	≥ 53
Willfact®	≥ 10	2%	2,1%	8 - 14		≥ 50

Obsah VWF:RCo ku VWF:Ag a FVIII:C v plazmatických koncentrátech

**Federici AB. Haemophilia 2006; 12, (Suppl. 3): 152-158.*

Table 2. Plasma-derived concentrates containing von Willebrand factor.

Concentrate	Purification procedures	Virucidal Rx	VWF:RCo/ Ag*	VWF:RCo/ FVIII*
Concentrates with published activity in VWD subjects				
Wilfactin	Ion exchange, affinity CTs	SD, nf, dry heat	0.7	60
Haemate-P†	Polyelectrolyte precipitations	Pasteurization	0.9	2.5
Wilate	Affinity CT, size exclusion	SD, dry heat	1.0	0.8
Alphanate	Heparin ligand CT	SD, dry heat	0.9	1.2
Fanhdi	Precipitation, heparin ligand CT	SD, dry heat	0.8	1.6
Concentrates with limited activity or no published studies in VWD subjects				
Emoclot	Ion exchange CT	SD, dry heat	0.6	1.2
Innobrand	Ion exchange CT	SD	0.8	2.5
Koate DVI	Precipitations, size exclusion	SD, dry heat	0.5	1.2
8Y	Heparin/glycine precipitation	Dry heat	0.3	0.8
Immunate	Ion exchange CT	SD, vapour heat	0.15	0.16

Koncentráty FVIII/VWF k léčbě VWCH

koncentrát	VWF:RCo/FVIII:C				
	*	♣	●	♦	SPC
Haemate P	2,5	2,5	2,54	2,0-2,7	2,4
Fanhdi	1,6	1,6	1,48	ND	1,2
Alfanate	1,2	1,6	ND	2,04	
Immunate	0,16	ND	1,1	1,67	0,75
Wilate	0,8				0,9
FVIII-VHP-vWF	ND	ND	ND	4,3 – 8,5	
Wilfactin	60	10	ND	8,75	>10

** Federici A.B., Haemophilia 2006* *♣ Lee A.L.,Textbook of Hemophilia, 2005*

● Federici A.B., Haemophilia 2002 *♦Berntorp E., Haemophilia 1999* ***SPC** údaje uvedené výrobcem*

Charakteristika Haemate P dle SPC a literatury

	VWF: RCo / FVIII	VWF: RCo / Ag	VWF:RCo		FVIII		VWF. RCo / 1 mg	FVIII IU / 1 mg
			%/IU/kg	t1/2	%/IU /kg	t1/2		
HAEMATE P	2,4		1,9	Střední 7,1 MRT10,3			3-17	2-6
	2,5***	0,91**	2,1*	11,3*	2,7*	24,6/**	15**	7,4**
	2,45*+	0,96++	1,9//	10,3//	2,7++*	20,5/**	10/	5/
		0,9***	1,7 /// T1	22///T1	2,4/**			
		0,59*+	2 /// T2A	15///T2A	2,7/**			
			2,5/// T3	8,8 ///T3				
			2,4++*	11,7++*				
			1,35/*	12,8/**				
			2,0/**	10,2/**				
			2,0/**					

Plazmatické koncentráty VWF dle SPC a literatury

	VWF: RCo / FVIII	VWF: RCo / Ag	VWF:RCo		FVIII		VWF: RCoIU /1 mg	FVIII IU / 1 mg
			%/ IU/kg	t1/2	%/IU /kg	t1/2		
Fanhdi	1,2 1,6*** 1,04*+ 1,01**+ 1,5+*	0,88++ 0,8*** 0,47*+ 0,72**+ 0,83+*	1,9 2,3****	14,4 9,5****	2,6	33,4	3-12 22/	2,5-10 20/
Immu-nate	0,75 0,16***	0,15** 0,47++ 0,15***					52,5 ! 6,9** 31/	70 ! 40,9** 24/
Wilate	0,9 0,8***	1,0***	1,52 1,9/** 2,1/**	18 15,8/** 9,1/**	2,2/** 2,5/**	19,6/** 16,1/**	≥ 53 75/	≥ 60 82/
Willfact Wilfac-tin	≥ 10 60***	0,7***	2,1 2,1*/+ 2,5*//	12 12,4*/+ 11,3*//	5,8%/h*/+ 5,8%/h*//		≥ 50 < 1/	11/

Použitá literatura

•Dobrovska A, Krzensk U, Chediak JR. Pharmacokinetics, efficacy and safety of Humate-P in von Willebrand dinase- Haemophilia 1998; 4 (Suppl. 3): 33-39.
** Lethagen S, Carlson M, Hillarp A. A imperative in vitro evaluation of six von Willebrand factor concentrates. Haemophilia 2004; 10: 243-249.
++ Federici AB. Highly purified VWF/FVIII concentrates in the treatment and prophylaxis of von Willebrand dinase: the PRO.WILL Study. Haemophilia 2007; 13 (Suppl. 5): 15-24.
/ Pock K, Stadler M, Gruber G et al. Biochemical comparison of VWF/FVIII concentrates used in VWD: are there differences in product characteristics? Haemophilie 2008; 14, (Suppl. 2): 13, abstrakt 03PO28.
//CSL Behring GmbH. Humate P, presribing information, revised October 2007, www.humate-p.com/pdf/HumateP_PI.pdf, Access 28 April 2008
*** Federici AB, Castaman G, Thompson A, Berntorp E. Von Willebrand´s dinase: clinical management. Haemophilia 2006; 12, (Suppl. 3): 152-158.
**** Hernandez F, Jimenez-Yuste V, Quintana M, Villar A. Effective replacement therapy in severe von Willebrand disease (VWD) with plasma derived FVIII/VWF concentrate (Fanhdi). XXV Internat. Conference of the World Federation of Haemophilia, Sevilla, May 2002.
*+ Mannucci PM, Franchini M, Castaman G et al. Evidence-based recommendation in the treatment of von Willebrand dinase in Italy. Blood Transf 2009; 7: 117-126. (vlastní analýza provedená v Milaně z 10 šarží)
**+ Instituto Grifols, n = 195 batches, April 2005
+* Instituto Grifols, lot No = IBVB6XDXB1, Juna 26th, 2009

Použitá literatura

/// Lethagen S, Kyrle PA, Castaman G etal. Von Willebrand factor/factor VIII concentrate (Haemate P) dosing based on pharmacokinetics: a prospective multicenter trial in elective sumery. J Thromb Haemost 2007; 5: 1420-30.

++* Gill JC, Shapiro A, Valentino LA et al. Von Willebrand factor/factor VIII concentrate (Humate-P) for management of elective surgery in adults and children with von Willebrans dinase. Haemophilia 2011; 17: 895-905.

*/+ Goudemand J, Scharrer I, Brntorp E et al. Pharmacokinetic studies on Wilfactin, a von Willebrand factor concentrate Roth low factor VIII contgent treated with free virus-inactivation/removal methods. J Thromb Haemost 2005; 3: 2219-27.

*// Menache D, Aronson DL, Darr F. Pharmacokinetics of von Willebrand facto and factor VIII in patiens with the severe von Willebrand dinase (type 3)¨estimation of the rate of factor VIII synthesis. Br J Haematol 1996; 94: 740-5.

*/+, *// recovery FVIII je hodnoceno nárůstem hladiny FVIII v %/hod.

/* Lillicrap D, Poon MC, Walker I et al. Efficacy and Safety of the Factor VIII/von Willebrand Factor Concentrate, Haemate-P/Humate-P: Ristocetin Cofactor Unit in Patients with von Willebrand Disease. Thromb Haemost 2002; 87: 224-30.

/** Kessler CM, Friedman K, Schwartz BA et al. The pharmacokinetic diversity of two von Willebrand factor (VWF)/factor VIII (FVIII) concentrates in subjects with congenital von Willebrand docease. Thromb Haemost 2011; 106: 279-288.

Dávkování substituce u VWCH

druh krvácení	cílová hladina		délka substituce
	VWF:RCo	FVIII:C	
velké operace	80-100%	kolem 100%	během zákroku
	> 50%	> 50%	do zhojení (7-10 dnů)
malé operace	> 50%	> 50%	během zákroku
	> 30-50%	> 30-50%	do zhojení (5-7 dnů)
zubní extrakce	> 50%	> 50%	během zákroku
	> 30%	> 30%	dalších 6-12 hod.
	+ antifibrinolytikum		7-10 dnů
krvácení (spont. i traumatické)	> 30%	> 30%	jednorázově či až do zhojení (2-4 dny)
vaginální porod	> 40-50%	> 40-50%	3 – 5 dnů

**Mannucci PM.Blood Transfus 2009;7:117-26 (Itálie)*
**Nordic Guidelines on VWD 2008 (Skandinávie)*
**Nichols WL. Haemophilia 2008;14:171-232 (USA)*
**Pasi KJ. Haemophilia 2004; 10: 218-231 (Velká Brit.)*

Obvyklé hladiny FVIII:C a VWF:RCo dle jednotlivých typů von Willebrandovy choroby

Individuals	FVIII:C (U/dl)	VWF:RCo (U/dl)	FVIII/VWF ratio
Normal	50 - 150	50 – 150	1
H.A.	<1 – 30	50 – 150	0.02-0.2
VWD 3	3 – 15	<1	3 – 15
VWD 2A	30 – 90	<3 – 9	10
VWD 2B	30 – 60	10 – 30	2 – 3
VWD 2M	30 – 60	<3 – 20	3 – 10
VWD 2N	10 – 30	30 – 60	0.3 – 0.5
VWD 1	9 – 120	<3 - 40	3

Haemostatic efficacy assessments by investigator for VWD patients in CDN study

	Type of VWD					
	1	2A	2B	Other	3	TOTAL
Surgeries						
No. events	26	6	14	6	21	73
Excellent/good	**100%**	**100%**	**93%**	**100%**	**100%**	**99%**
% Poor/none			7%			1%
Bleedings						
No. events	32	17	60	27	208	344
Excellent/good	**100%**	**100%**	**100%**	**93%**	**95%**	**97%**
Poor/none				7%	5%	3%
Other						
No. events	6		14	7	66	93
Excellent/good	**67%**		**100%**	**71%**	**86%**	**86%**
Poor/none					8%	5%
Not available	33%			29%	6%	9%
Prophylaxis						
No. events					20	20
Excellent/good					**100%**	**100%**

** Schramm W. European Journal of Haematology 2008; 80 (Suppl. 70: 3-35*

Overall haemostatic efficacy assessments by investigator for VWD patients in A4001 study

	No. treatment events	No. days with treatment	No. (%) treatmentevents	
			Excellent/ good	Fair/ poor
Overall	101	950	100 (99.0)	1 (1.0)
Serious bleeding	53	232	52 (98.1)	1 (1.9)
Surgery	39	253	39 (100)	
Prophylaxis	9	465	9 (100)	

** Schramm W. European Journal of Haematology 2008; 80 (Suppl. 70: 3-35*

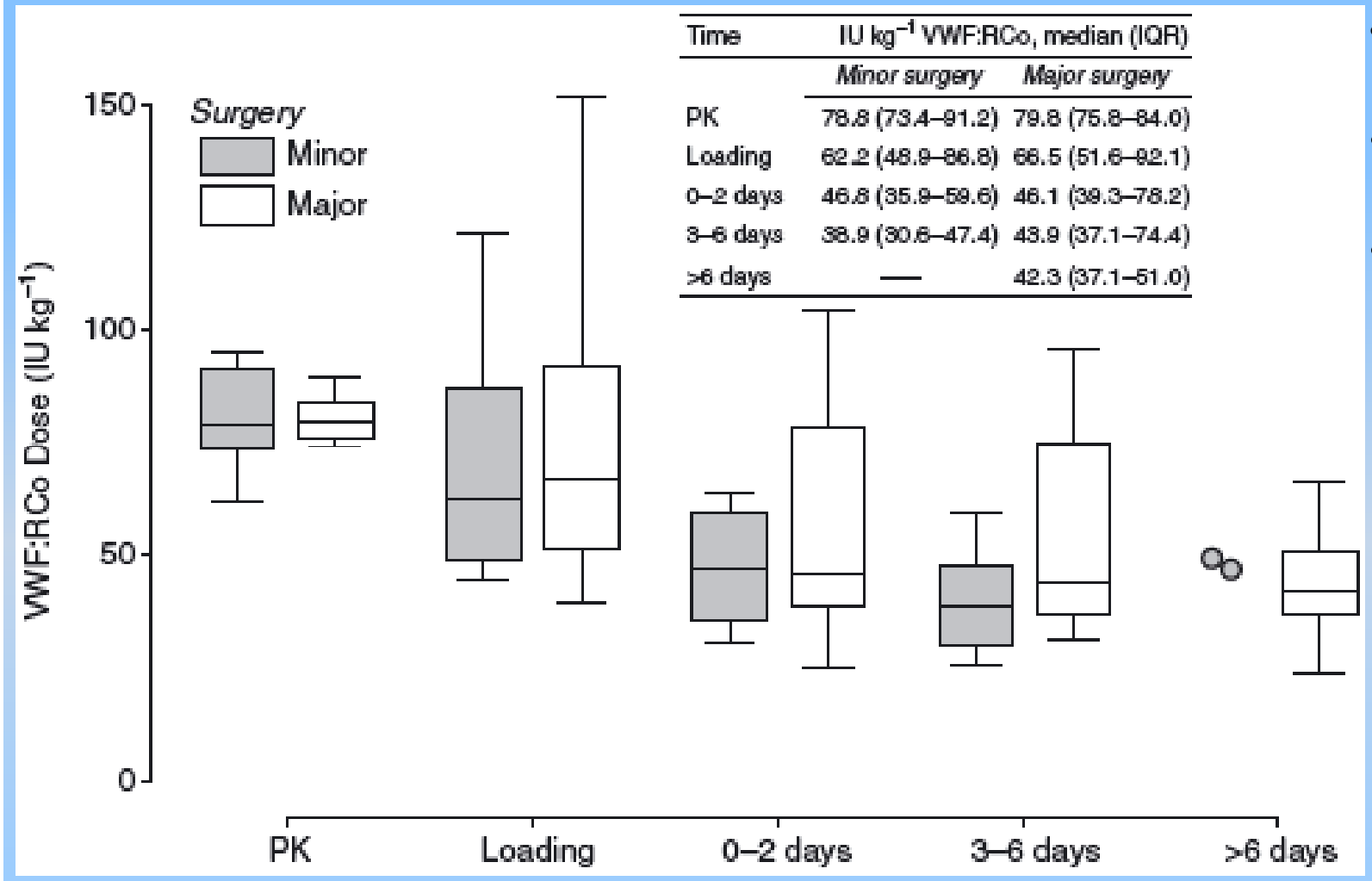
von Willebrand factor/factor VIII concentrate (Haemate® P) dosing based on pharmacokinetics: a prospective multicenter trial in elective surgery

S. LETHAGEN,* P. A. KYRLE,† G. CASTAMAN,‡ S. HAERTEL,§ P. M. MANNUCCI,¶ FOR THE HAEMATE P® SURGICAL STUDY GROUP

VWF:RCo < 10%

<u>Účinnost excellent / good:</u>

- operace:
  - 96%
- 2. den:
  - 100%:
- 14. den:
  - 100%



Time	IU kg^{-1} VWF:RCo, median (IQR)	
	Minor surgery	*Major surgery*
PK	78.8 (73.4–91.2)	79.8 (75.8–84.0)
Loading	62.2 (48.9–86.8)	66.5 (51.6–92.1)
0–2 days	46.8 (35.9–59.6)	46.1 (39.3–76.2)
3–6 days	38.9 (30.6–47.4)	43.9 (37.1–74.4)
>6 days	—	42.3 (37.1–51.0)

Trombembolické komplikace (Haemate P)

7 případů na 12 640 roků léčby

** Schramm W. European Journal of Haematology 2008; 80 (Suppl. 70: 3-35*

- VWF:Rco a FVIII:C > 100%
  - většinou FVIII:C > 200% **Nichols WL. Haemophilia 2008;14:171-232 (USA)*
  - NHLBI guidelines:
    - VWF:RCo < 200%
    - FVIII:C < 250-300%
- Většina:
  - perioperačně
  - bez profylaxe TEN
- Doporučení:
  - standardně profylaxe TEN

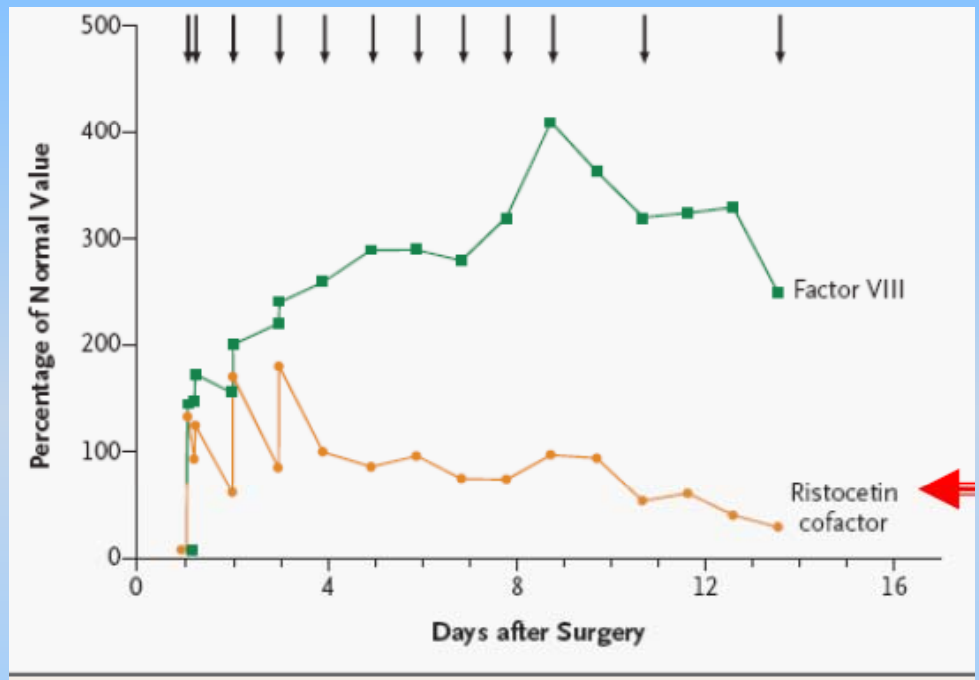


Figure 3. Representative Example of the Changes of Plasma Levels in Ristocetin Cofactor Activity and Factor VIII Coagulant Activity in a Patient with Type 3 von Willebrand's Disease.

** Mannuci PM.N Engl J Med 2004; 351: 6683-94*

Haemophilia (2010), **16**, 101–110 DOI: 10.1111/j.1365-2516.2009.02088.x

ORIGINAL ARTICLE *von Willebrand disease*

Efficacy and safety of highly purified, doubly virus-inactivated VWF/FVIII concentrates in inherited von Willebrand's disease: results of an Italian cohort study on 120 patients characterized by bleeding severity score

A. B. FEDERICI,* G. BARILLARI,† E. ZANON,‡ M. G. MAZZUCCONI,§ R. MUSSO,¶ R. TARGHETTA** and P. M. MANNUCCI*

*Angelo Bianchi Bonomi Hemophilia Thrombosis Center, Department of Medicine and Medical Specialties, IRCCS

Parameter, median (range)	All VWD patients (n = 120)	VWD1 (n = 56)	VWD 2A (n = 19)	VWD2B (n = 25)	VWD2M* (n = 10)	VWD3 (n = 10)
Gender (M/F)	51/69	22/34	7/12	8/17	8/2	6/4
Age (years)	50 (6–83)	48 (7–83)	50 (25–82)	36 (6–79)	64 (21–80)	57 (30–72)
Weight (kg)	70 (17–95)	68 (25–95)	70 (48–90)	63 (17–87)	77 (58–90)	70 (64–93)
Bleeding severity score	8 (0–27)	8 (0–22)	8 (0–23)	7 (2–27)	9 (2–17)	16 (6–22)
VWF:RCo (IU dL^{-1})	20 (<3–56)	33 (3–56)	6 (<3–40)	15 (<3–52)	4 (<3–22)	< 3
VWF:Ag (IU dL^{-1})	35 (<3–88)	39 (4–80)	22 (1–60)	45 (11–88)	13 (5–38)	< 3
FVIII:C (IU dL^{-1})	41 (2–129)	46 (12–99)	30 (10–100)	59 (18–129)	29 (15–76)	5 (2–17)

Efficacy and safety of highly purified, doubly virus-inactivated VWF/FVIII concentrates in inherited von Willebrand's disease: results of an Italian cohort study on 120 patients characterized by bleeding severity score

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VWD1	VWD2A	VWD2B	VWD2M	VWD3
$n = 22$	$n = 10$	$n = 13$	$n = 3$	$n = 7$

	No of infusion	Dosage (RCo kg^{-1} day^{-1})	Total dose IU VWF:RCo	Outcome Good/ Excellent
	Median (range)	Median (range)	Median (range)	n (%)
All bleedings	2 (1–40)	40 (11–124)	5138 (685–189 060)	111 (97)
By anatomical site				
Epistaxis	1 (1–5)	48 (20–70)	4,110 (685–31 510)	22 (100)
Gastrointestinal	2 (1–31)	47 (13–88)	8,220 (2,740–189 060)	16 (84)
Gums	2	39	5480 (5480)	1 (100)
Meno-methrorragia	3 (1–6)	59 (17–90)	8,220 (1370–30 140)	13 (100)
Cerebral haemorrhage	40	11	27 400 (27 400)	1 (100)
Wound bleeding	15 (1–23)	25 (23–42)	30 140 (1370–64 390)	3 (100)
Ecchymosis/Haematomas	2 (1–11)	37 (21–76)	2740 (1370–16 440)	27 (100)
Haemarthrosis	2 (1–7)	38 (17–68)	3425 (1370–38 360)	14 (100)
Other sites	4 (1–17)	39 (17–124)	10 960 (1370–30 140)	14 (100)

Efficacy and safety of highly purified, doubly virus-inactivated VWF/FVIII concentrates in inherited von Willebrand's disease: results of an Italian cohort study on 120 patients characterized by bleeding severity score

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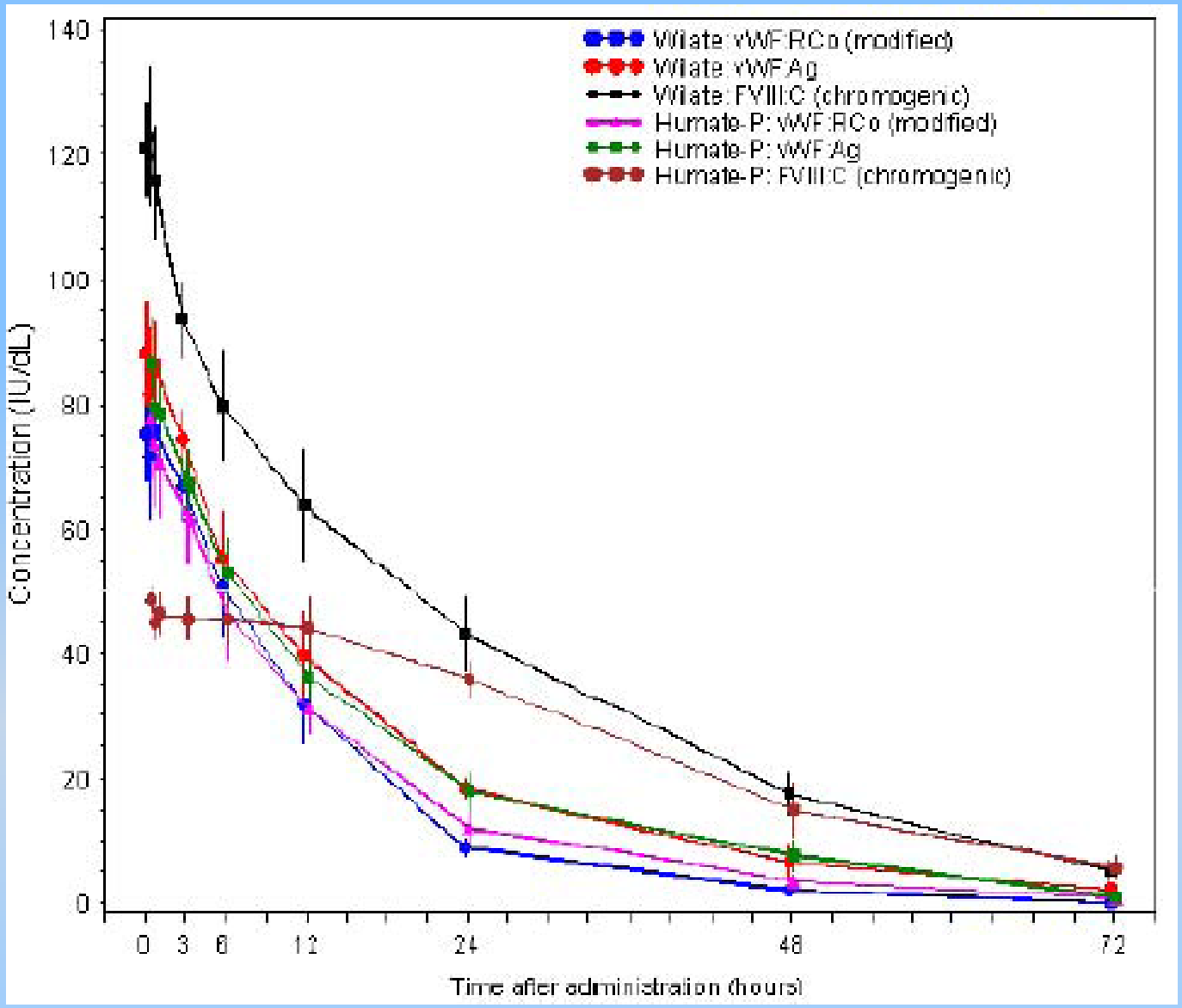
VWD1	VWD2A	VWD2B	VWD2M	VWD3
$n = 44$	$n = 15$	$n = 13$	$n = 9$	$n = 4$

	No. of infusions	Preoperative dose (IU RCo kg^{-1})	Treatment dose (IU RCo kg^{-1} per die)	Total dose(IU VWF:RCo	Outcome Good/ Excellent
	Median (range)	Median (range)	Median (range)	Median (range)	N (%)
All procedures	2 (1–37)	48 (11–137)	44 (14–98)	5,480 (685–200 020)	130 (99)
by type:					
Major surgery	6 (1–37)	62 (17–137)	51 (14–98)	12,330 (2740–200 020)	45 (100)
Invasive procedures	3 (1–11)	52 (17–73)	42 (14–68)	10,618 (4110–42 470)	24 (100)
Dental	1 (1–5)	44 (11–82)	39 (20–64)	4110 (685–12,330)	57 (100)
Delivery	3 (1–8)	59 (38–68)	40 (38–63)	9590 (2740–28 770)	4 (99)*

Farmakokinetika Haemate P - Wilate



** Kessler CM. Thromb Haemost 2011; 106: 279-288*

Farmakokinetika Haemate P - Wilate

Typ 3 N = 6	IVR % / IU / kg průměr		T1/2 Terminal (h) průměr		T1/2 Průměrný (h) průměr		MRT (h) průměr	
	Willate	Humate P	Willate	Hmate P	Willate	Humate P	Willate	Humate P
VWF: Rco	2,07	2,01	9,1	10,2	9,5	9,0	11,9	13,8
FVIII:C chrom.	2,47	2,69	16,1	20,5	13,0	35,7	23,0	30,3

** Kessler CM. Thromb Haemost 2011; 106: 279-288*

Treatment and prevention of acute bleedings in von Willebrand disease – efficacy and safety of Wilate®, a new generation von Willebrand factor/factor VIII concentrate

E. BERNTORP,* J. WINDYGA† and THE EUROPEAN WILATE STUDY GROUP
*Malmö University Hospital, Malmö Centre for Thrombosis and Haemostasis, Malmö, Sweden; and †Institute of Haematology and Transfusion Medicine, Warsaw, Poland

Table 1. Demographic characteristics and bleeding frequency before study entry of the 44 patients included in the Europea

		VWD type 2			
	VWD type 1	2A	2B	2N	VWD type 3
Number of individuals (*n*)	8	6	4	2	24
Male/female (*n*)	4/4	1/5	2/2	1/1	12/12
Mean age, years (range)	34.9 (5–63)	43 (10–73)	54 (35–65)	25 (25–25)	24.9 (6–56)
Mean body weight, kg (range)	58 (19–70)	67 (26–80)	78 (63–88)	64 (63–65)	60 (23–104)
Mean number of BEs per month before study entry (range)	1.5 (0.1–8)	1.9 (0.25–4)	4.6 (1–8)	0.17 (0.08–0.25)	4.2 (0.2–28)
Mean VWF:RCo baseline, % (range)	50 (12–95)	35 (14–63)	27 (12–42)	80 (63–97)	4 (1–14)
Mean VWF:Ag baseline, % (range)	49 (12–108)	80 (22–183)	58 (30–116)	90 (84–96)	<5*
Mean FVIII:C baseline, % (range)	46 (5–78)	68 (35–135)	59 (36–117)	4 (3–5)	3 (0–16)

BE, bleeding episode.
*5% was the limit of quantification.

Treatment and prevention of acute bleedings in von Willebrand disease – efficacy and safety of Wilate®, a new generation von Willebrand factor/factor VIII concentrate

E. BERNTORP,* J. WINDYGA† and THE EUROPEAN WILATE STUDY GROUP

Site of bleeding	No. of treated BEs	Mean dose per treatment day ± SD (IU kg^{-1})	Mean no. of treatment days ± SD Median (range)	Excellent/good efficacy (%)
Joints	565	28 ± 12	1.67 ± 1.08 1 (range 1–8)	99
Epistaxis	94	27 ± 12	1.52 ± 0.94 1 (range 1–5)	94
Gastrointestinal	145	44 ± 20	4.23 ± 4.31 3 (range 1–29)	82
Oral	34	26 ± 12	1.82 ± 2.96 1 (range 1–17)	94
Menorrhagia	62	36 ± 12	1.35 ± 0.70 1 (range 1–4)	97
Other (muscle, soft tissue)	195	23 ± 11	1.39 ± 0.98 1 (range 1–9)	99
Total	1095	29 ± 15	1.93 ± 2.10 1 (range 1–29)	96

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	VWD type 1 (29 BEs)	VWD type 2 (64 BEs)	VWD type 3 (1002 BEs)	Total (1095 BEs)
No. of treatment days per bleeding episode				
Mean ± SD	1.24 ± 0.64	3.97 ± 5.15	1.82 ± 1.68	1.93 ± 2.1
Median (range)	1 (1–3)	1 (1–29)	1 (1–23)	1 (1–29)
Average dose (IU kg^{-1}) per treatment day				
mean ± SD	28 ± 7	36 ± 15	29 ± 15	29 ± 15
median (range)	25 (22–49)	31 (13–78)	24 (9–113)	26 (9–113)
Loading dose (IU kg^{-1}) per treatment day				
Mean ± SD	28 ± 7	38 ± 17	30 ± 15	30 ± 15
Median (range)	25 (22–49)	32 (13–95)	26 (9–113)	26 (9–113)
Maintenance dose (IU kg^{-1}) per treatment day				
Mean ± SD	23 ± 0	38 ± 14	25 ± 16	26 ± 16
Median (range)	23 (23–23)	34 (13–69)	20 (6–92)	22 (6–92)

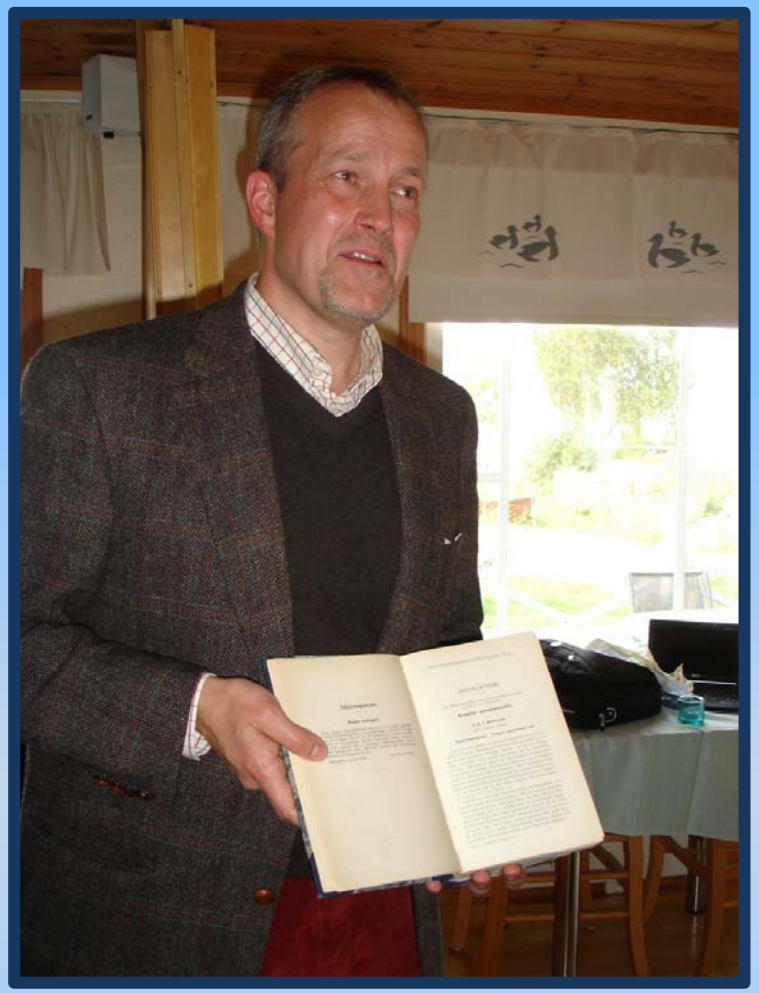
Profylaktická léčba VWCH

- sekundární profylaxe
- indikace:
  - typ 2, 3
  - recidivující hemartros
  - GIT
  - epistaxe
  - menoragie
- 10 - 50 IU FVIII 1-3 x týdně (Haemate P®)

** Berntorp E. Haemophilia 2008; 14 (Suppl.5): 47-53*

HP VWF (Wilfactin®)

- maximum vzestupu FVIII:C za 6 - 24 hod.
  - u akutního krvácení kombinovat s koncentrátem FVIII
- před operacemi první dávka 12 hod. předem:
  - t2 VWF:RCo = 11 hod.
  - t2 FVIII:C = 17 hod.



Děkuji za pozornost !

evropský sociální fond v ČR

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OP Vzdělávání pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ