dr. rott
dr. halimeh
dr. kappert

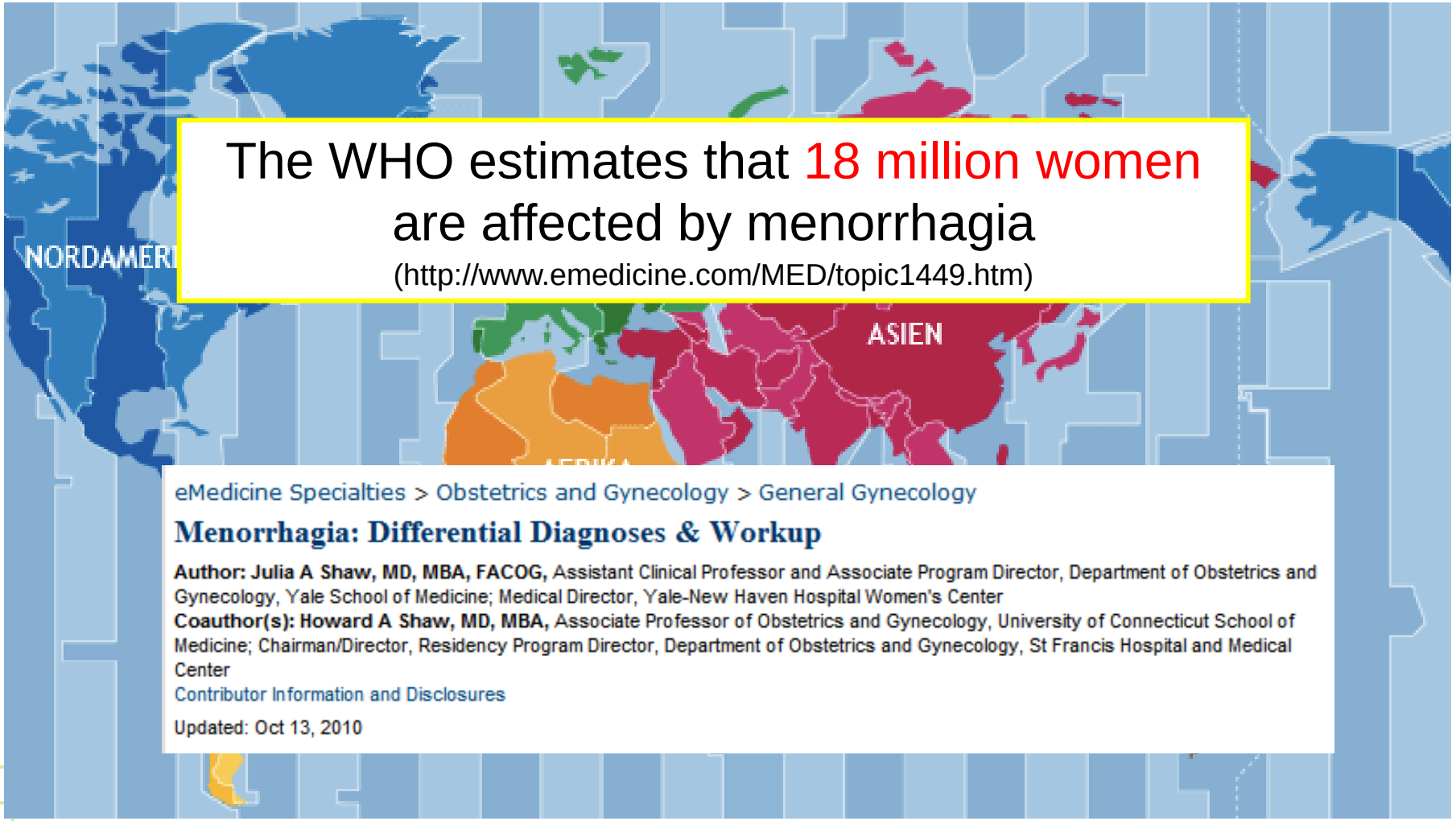
gerinnungs
zentrum
rhein-ruhr

Menorrhagia and postpartum haemorrhage in women with rare bleeding disorders

Dr. med. Susan Halimeh

The WHO estimates that 18 million women are affected by menorrhagia

(http://www.emedicine.com/MED/topic1449.htm)



eMedicine Specialties > Obstetrics and Gynecology > General Gynecology

Menorrhagia: Differential Diagnoses & Workup

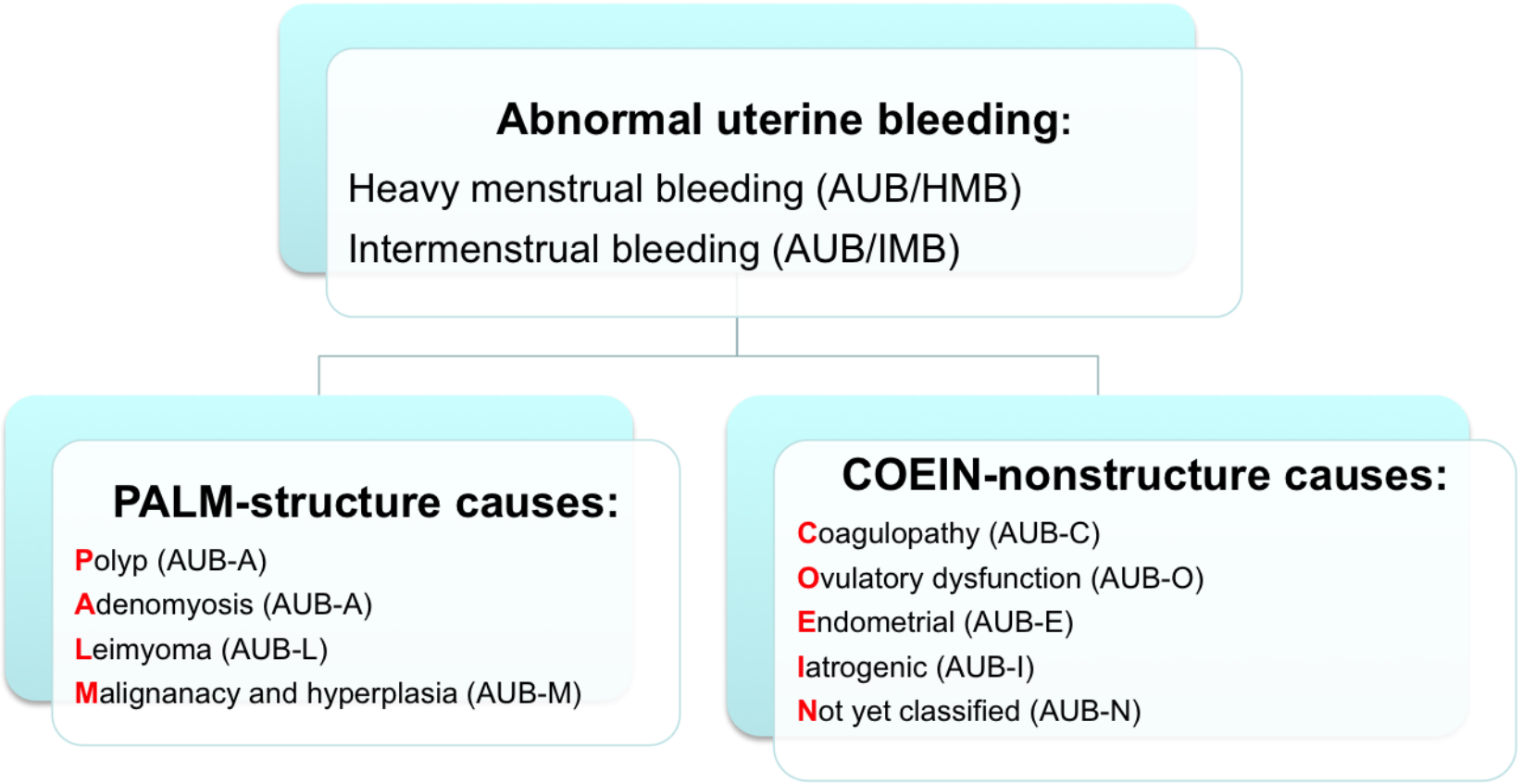
Author: Julia A Shaw, MD, MBA, FACOG, Assistant Clinical Professor and Associate Program Director, Department of Obstetrics and Gynecology, Yale School of Medicine; Medical Director, Yale-New Haven Hospital Women's Center

Coauthor(s): Howard A Shaw, MD, MBA, Associate Professor of Obstetrics and Gynecology, University of Connecticut School of Medicine; Chairman/Director, Residency Program Director, Department of Obstetrics and Gynecology, St Francis Hospital and Medical Center

Contributor Information and Disclosures

Updated: Oct 13, 2010

Etiologies of acute abnormal uterine bleeding



FIGO Working Group on Mentrual disorders. Int J Gynaecol Obstet 2011; 113:3-13

- **Heavy menstrual bleeding since menarche**
- **One of the following conditions:**
  - Postpartum hemorrhage
  - Surgery- related bleeding
  - Bleeding associated with dental work
- **Two or more of the following conditions:**
  - Bruising, one to two times per month
  - Epistaxis, one to two times per month
  - Frequent gum bleeding
  - Family history of bleeding symptoms

Modified from Kouides PA, Conrad J, Peyvandi F, Lukes A, Kadir R. Fertil Steril 2005; 84: 1345-51

Women with bleeding disorders- Menorrhagia

Iron deficiency anaemia

64% in women with bleeding disorders Vs 34% control

Kadir et al 1999, Kouides et al 2000

Symptoms:
Tiredness
Fatigue
Loss of power

FBC and Ferritin assessment

Predictors for underlying bleeding disorders

Clinical anaemia – odd ratio 3.3
Low ferritin - predict 60% of MBL>80ml
-Odd ratio 51 for Iron deficiency anaemia

Jayasinghe et al 2005, Warner et al 2004

Menorrhagia- Definition

Excessive or prolonged uterine bleeding that exceeds 80 mL of blood loss per menstruation (in the presence of a normal secretory endometrium after normal ovulation)

Valle RF and Sciarra JJ. In: Menorrhagia. Oxford: Isis Medical Media, 1999

Normal menstrual cycle

25–35 days in duration, with bleeding lasting an average of 5 days and total blood flow between 25 and 80 mL

Menorrhagia

A blood loss of greater than 80 ml per menstrual cycle or lasting longer than 7 days

Lentz GM, Abnormal Uterine Bleeding. In Katz VL, Lentz GM Comprehensive Gynecology5Th 2007; 915-932

Definition of Menorrhagia



Length of menstruation period

Table I. Characteristics of menstruation in the study groups*.

	Healthy adult women	Healthy teenage girls	Healthy adults and teenage girls	Healthy on OCP	Untreated menorrhagic women	Menorrhagic women on OCP	Teenage girls claiming heavy menses
Number	26	52	78	7	17	5	6
Age	35 (37; 24–46)	17 (16; 16–18)	23 (17; 16–46)	24 (26; 16-28)	39 (38; 31–49)	30 (29; 16–45)	16 (16; 16–16)
Measured menstruation length (days)	5 (5; 3–8)	5 (6; 3–7)	5 (5; 3–8)	4 (4; 2–5)	7 (6; 4–12)	5 (5; 4–7)	6 (6; 5–8)
Protective pad number	13 (16; 4–27)	14 (13; 5–33)	14 (13; 4–33)	8 (8; 5–12)	26 (24; 12–44)	13 (14; 9–16)	15 (13; 8–25)
History of diagnosed iron deficiency	3/26	4/52	7/78	2/7	14/17	4/5	3/6

*Results are shown as mean (median; range).

Brynja R. Gudmundsdottir et al. Quantification of menstrual flow by weighing protctive pads in women with normal, decreased or increased mentruation Acta Obstrtricia et Gynecologica 2009, 1-5

Menorrhagia- Definition

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Prevalence of VWD in adolescents with menorrhagia

Tab. 1 Prevalence studies in bleeding disorders associated with menorrhagia in adolescents

study (ref.)	n	setting	VWD (%)
Chi et al. 2010 (22)	42	haemophilia treatment centre	20
Mikhail et al. 2007 (19)	61	outpatient haematology clinic	36
Jaysainghe et al. 2005 (17)	106	inpatient and outpatient	5
Philipp et al. 2004 (12)	25	outpatient primary care clinic	4
Kanbur et al. 2004 (18)	47	inpatient	4
Bevan et al. 2001(14)	71	emergency department, urgent care and inpatient	3
Oral et al. 2001 (20)	25	inpatient	8
Smith et al. 2001 (21)	46		5
Falcone et al. 1994 (16)	61		0
Claessens et al. 1981 (15)	59		8

Prevalence 3-36%

Haemophilia

Haemophilia (2011), **17** (Suppl. 1), 6–13 DOI: 10.1111/j.1365-2516.2011.02558.x

ORIGINAL ARTICLE

Surveillance of female patients with inherited bleeding disorders in United States Haemophilia Treatment Centres

V. R. BYAMS,* P. A. KOUIDES,† R. KULKARNI,‡ J. R. BAKER,§ D. L. BROWN,¶ J. C. GILL,** A. M. GRANT,* A. H. JAMES,†† B. A. KONKLE,‡‡ J. MAAHS,§§ M. M. DUMAS,¶¶ S. McALISTER,* D. NANCE,‡‡ D. NUGENT,*** C. S. PHILIPP,††† J. M. SOUCIE* and E. STANG,‡‡‡ and the Haemophilia Treatment Centres Network Investigators

N= 319

Table 3. Frequency of bleeding symptoms and provider intervention (n = 319).

	n (%) reported symptom	n (%) required provider intervention
More than one nosebleed per year lasting 10 min or longer	154 (48.4)	75 (48.7)
Oral mucosal bleeding lasting 10 min or longer	93 (29.4)	43 (46.2)
Bleeding during or after dental procedures of concern to healthcare provider	111 (35.1)	73 (65.8)
Bleeding from minor cuts lasting 5 min or longer	153 (48.0)	23 (15.0)
Bruising larger than a dime in a pattern that at least once occurred without trauma	174 (54.5)	13 (7.5)
Bleeding after surgery of concern to health care provider	119 (37.3)	102 (85.7)
Menstrual bleeding that required protection change at least every 2 h on heaviest day*	165 (76%)	95 (57.6)
Bleeding during pregnancy and/or postpartum of concern to health care provider†	63 (52.9)	51 (81.0)
Joint bleeding	51 (16.0)	37 (72.5)
Muscle bleeding	28 (8.8)	13 (46.4)
CNS bleeding	9 (2.8)	7 (77.8)
GI bleeding	37 (11.6)	23 (62.6)

Menstrual bleeding that required protection change at least every 2h 165 (76%)

© Schattauer 2011

Gynaecological and obstetric bleeding in moderate and severe von Willebrand disease

Eva M. de Wee[1]; H. Marieke Knol[2,3]; Eveline P. Mauser-Bunschoten[4]; Johanna G. van der Bom[5,6]; Jeroen C. J. Eikenboom[5,7]; Karin Fijnvandraat[8]; Arja de Goede-Bolder[9]; Britta Laros-van Gorkom[10]; Paula F. Ypma[11]; Sonja Zweegman[12]; Karina Meijer[2]; Frank W. G. Leebeek[1]; for the WiN study group

[1]Hematology, Erasmus University Medical Center Rotterdam, Netherlands; [2]Hematology, University Medical Center Groningen, Netherlands; [3]Gynaecology, University Medical Center Groningen, Netherlands; [4]Van Creveldkliniek and Hematology, University Medical Center Utrecht, Netherlands; [5]Einthoven Laboratory for Experimental Vascular Medicine, Leiden University Medical Center, Netherlands; [6]Department of Clinical Epidemiology, Leiden University Medical Center, Netherlands; [7]Thrombosis and Hemostasis, Leiden University Medical Center, Netherlands; [8]Pediatric Hematology, Emma Children's hospital AMC, Amsterdam, Netherlands; [9]Pediatrics, Erasmus MC, Sophia Children's hospital, Rotterdam, Netherlands; [10]Hematology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [11]Hematology, HagaZiekenhuis, The Hague, Netherlands; [12]Hematology, VU University Medical Center, Amsterdam, Netherlands

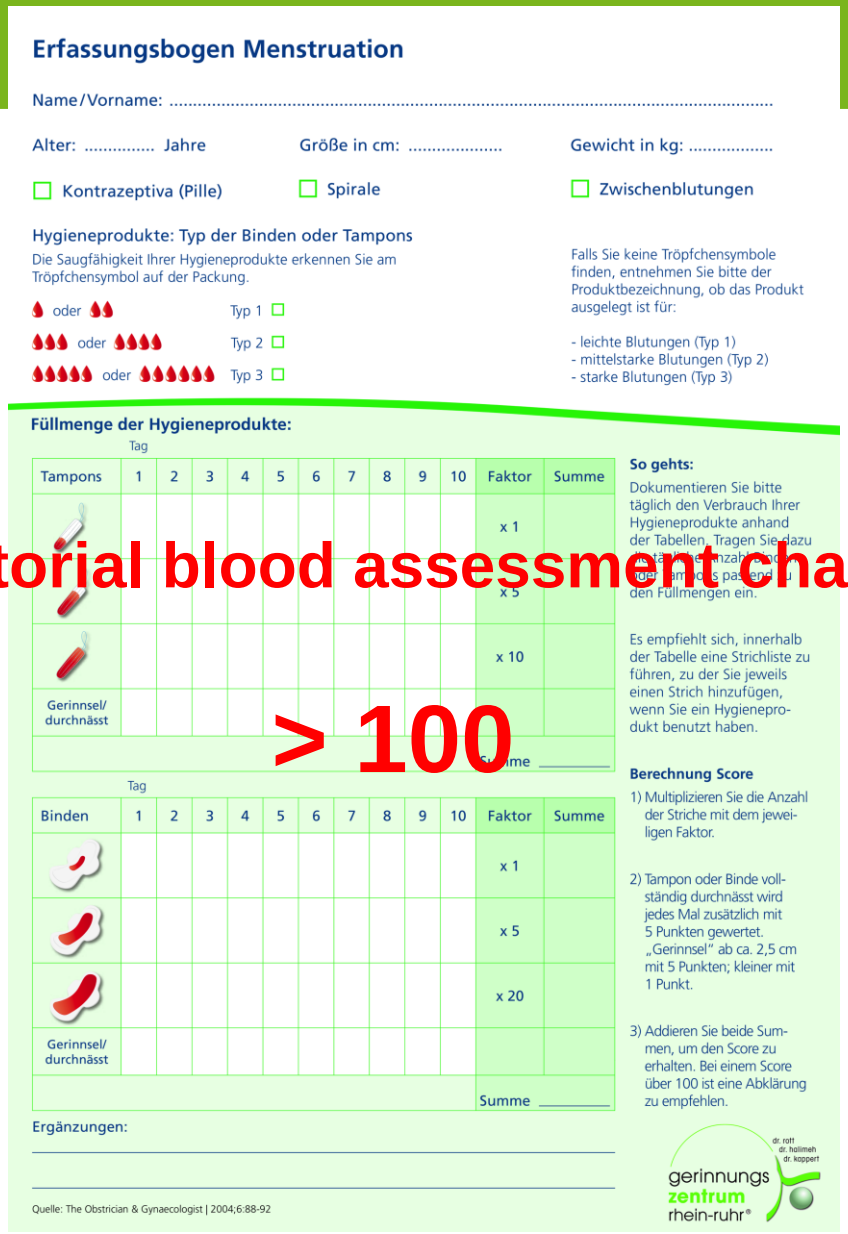
N= 378

Table 3: Menorrhagia in women with moderate or severe VWD.

		Total (n=423)		Type 1 (n=242)		Type 2 (n=120)		Type 3 (n=16)		P-value*
Age of menarche	median, IQR	13	12–14	13	12–14	13	12–14	13	12–14	0.63
Duration period	median, IQR	7	6–8	7	6–8	7	6–8	7	7–10	0.76
Number of days heavy menstrual bleeding	median, IQR	4	3–5	4	3–6	4	3–5	4	3–6.5	0.41
Menorrhagia symptoms	median, IQR	3	2–4	3	2–4	3	2–4	3	1–4	0.52
Excessive menstrual bleeding	n, %	347	82%	202	83%	98	82%	13	81%	0.19
Loss of blood clots	n, %	338	80%	196	81%	100	83%	10	63%	0.48
Requirement of iron or blood transfusion	n, %	184	44%	105	43%	60	50%	10	63%	0.08
Heavy menstrual flow that interferes with daily life	n, %	192	45%	110	45%	58	48%	7	44%	0.77
Menstrual period that lasts > 7 days	n, %	150	36%	81	33%	51	43%	6	38%	0.16
Menorrhagia ≥2 symptoms present	n, %	342	81%	196	81%	99	83%	12	75%	0.76
Menorrhagia severity	median, IQR	3	2–4	3	2–4	3	2–4	3	2–4	0.10
0: no menorrhagia	n, %	64	15%	41	17%	13	11%	1	6%	
1: consultation only	n, %	29	7%	19	8%	5	4%	1	6%	
2: antifibrinolytics or pill use	n, %	98	23%	46	19%	31	26%	5	31%	
3: dilatation and currettage or iron therapy	n, %	121	29%	74	31%	37	31%	3	19%	
4: blood transfusion, FVIII/VWF concentrate, desmopressin or hysterectomy	n, %	111	26%	62	26%	34	28%	9	56%	

* Chi square or ANOVA test for differences between subgroups. IQR, interquartile range.

Excessive menstrual bleeding 83% 82% 81%



Erfassungsbogen Menstruation

Name/Vorname: .....

Alter: ..... Jahre Größe in cm: ..... Gewicht in kg: .....

☐ Kontrazeptiva (Pille) ☐ Spirale ☐ Zwischenblutungen

Hygieneprodukte: Typ der Binden oder Tampons

Die Saugfähigkeit Ihrer Hygieneprodukte erkennen Sie am Tröpfchensymbol auf der Packung.

oder Typ 1 ☐

oder Typ 2 ☐

oder Typ 3 ☐

Falls Sie keine Tröpfchensymbole finden, entnehmen Sie bitte der Produktbezeichnung, ob das Produkt ausgelegt ist für:

- leichte Blutungen (Typ 1)
- mittelstarke Blutungen (Typ 2)
- starke Blutungen (Typ 3)

Füllmenge der Hygieneprodukte:

Tag

Tampons	1	2	3	4	5	6	7	8	9	10	Faktor	Summe
											x 1	
											x 5	
											x 10	
Gerinnsel/ durchnässt												

Summe _____

Tag

Binden	1	2	3	4	5	6	7	8	9	10	Faktor	Summe
											x 1	
											x 5	
											x 20	
Gerinnsel/ durchnässt												

Summe _____

Ergänzungen:

Quelle: The Obstrician & Gynaecologist | 2004;6:88-92

So gehts:

Dokumentieren Sie bitte täglich den Verbrauch Ihrer Hygieneprodukte anhand der Tabellen. Tragen Sie dazu [illegible] ein.

Es empfiehlt sich, innerhalb der Tabelle eine Strichliste zu führen, zu der Sie jeweils einen Strich hinzufügen, wenn Sie ein Hygieneprodukt benutzt haben.

Berechnung Score

1) Multiplizieren Sie die Anzahl der Striche mit dem jeweiligen Faktor.

2) Tampon oder Binde vollständig durchnässt wird jedes Mal zusätzlich mit 5 Punkten gewertet. „Gerinnsel" ab ca. 2,5 cm mit 5 Punkten; kleiner mit 1 Punkt.

3) Addieren Sie beide Summen, um den Score zu erhalten. Bei einem Score über 100 ist eine Abklärung zu empfehlen.

gerinnungszentrum rhein-ruhr®

Pictorial blood assessment chart

> 100

96% sensitivity

- The PBAC shows a number of diagrams representing:
- towels: lighty, moderate and heavily soiled
- tampons: lightly, moderate and heavily soiled
- clots/flooding: record the size of passaged clots, episodes of flooding
- Days of menstruation (if insufficient, add more days)

Higham JM et al. Assessment of menstrual blood loss using a pictorial chart. Br. J Obstet Gynecol 1990; 97: 737-9

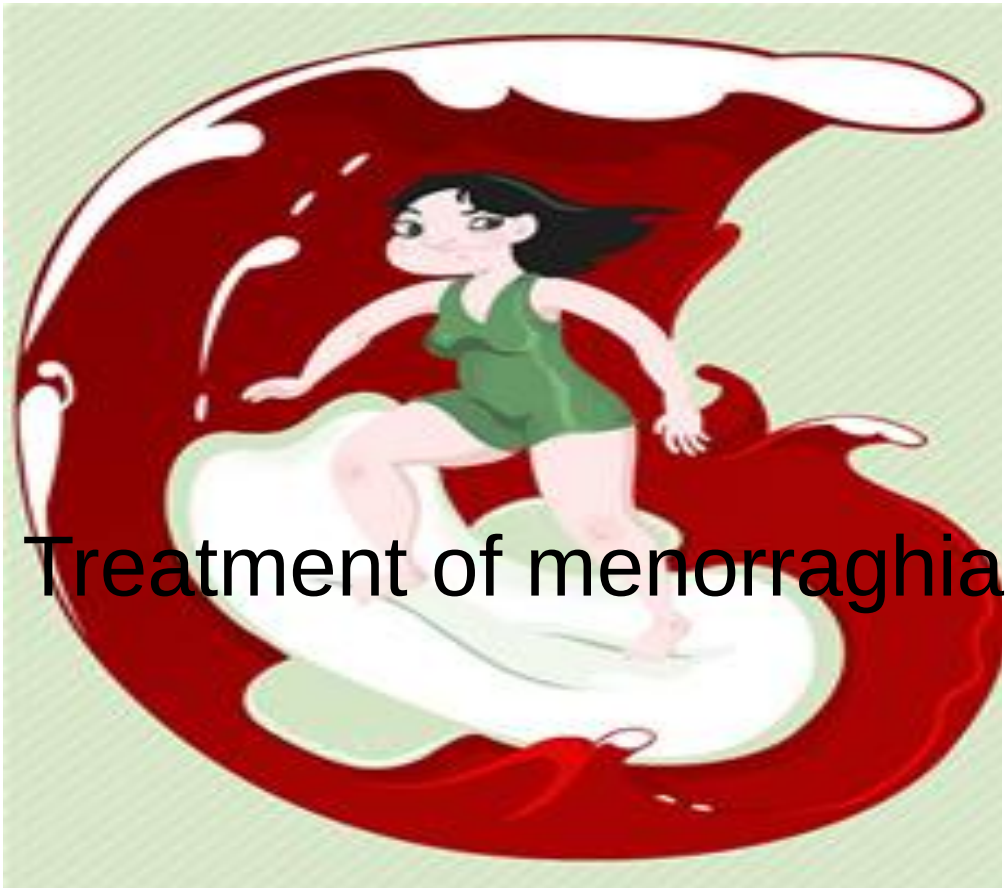
Our own study

- 305 females, 199 with menorrhagia, 105 controls
- age 11 – 56 years were included
  - Menarche since 2 years was required*
- PBAC-Score 31 - 4212 (Median 266)
- The following tests were conducted:
  - VWF:RCo, VWF:Ag, VWF:CB,
  - Fibrinogen (Clauss),
  - Activity tests for FII, FV, FVII, FVIII (clotting und chromogen), FIX, FX, FXI, FXII and FXIII

*because of anovulatory cycles

Diagnosis of coagulation disorders (Total cohort n = 305)

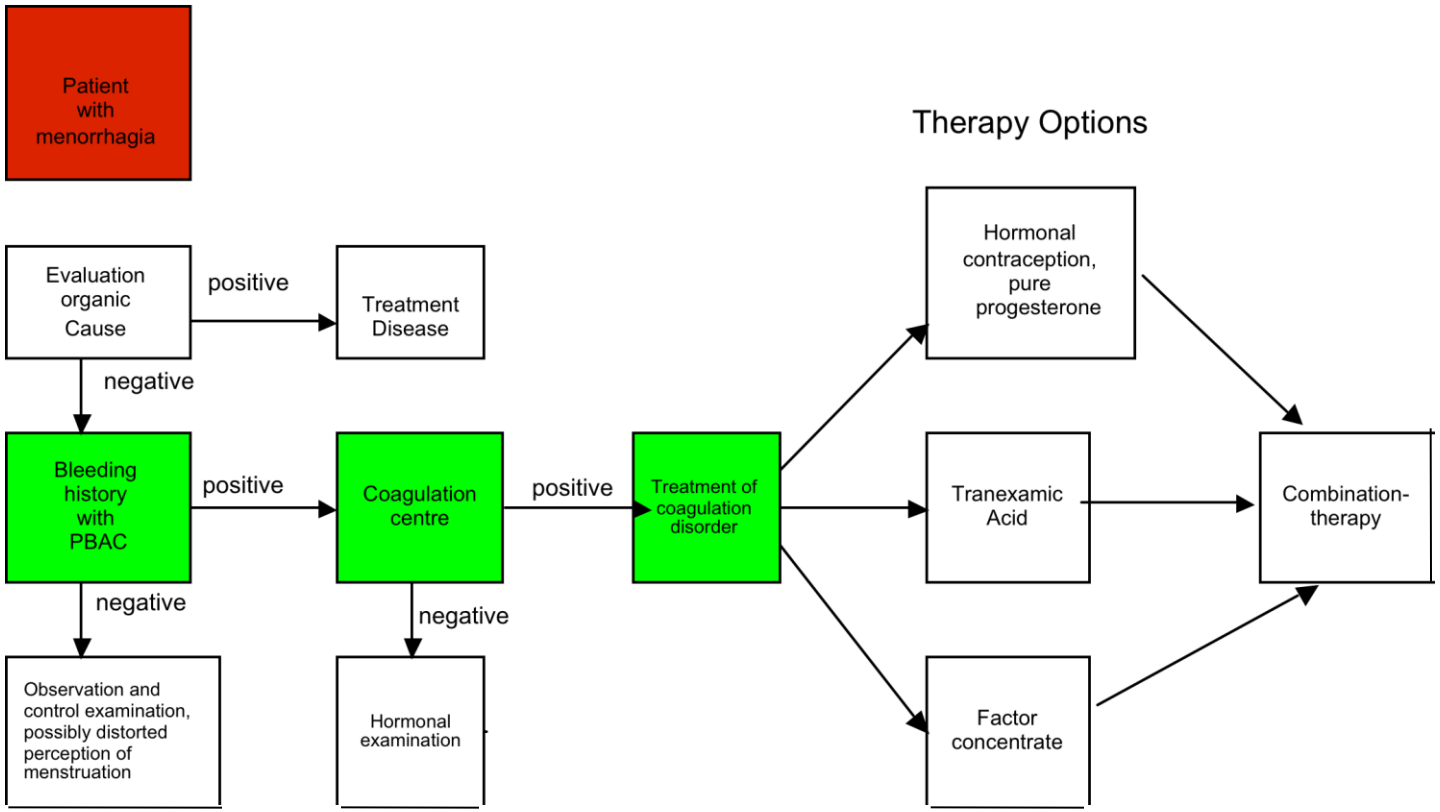
	Menorrhagia group n=199	Control group n=106
Age, years (range)	22 (11–56)	29 (13–54)
Age at menarche, years (range)	13 (9–25)	13 (10–23)
Age groups, n (%): **<20 years** **20–44 years** **≥45 years**	 93 (47) 96 (48) 10 (5)	 22 (21) 78 (74) 6 (6)
Length of menstrual cycle, days (range)	27 (17–35)	28 (25–32)
Duration of menstruation, days (range)	7 (3–19)	5 (1–9)
Bleeding symptoms, n (%) **Epistaxis** **Easy bruising** **Excessive bleeding during/after surgery** **Bleeding with tooth extraction**	 42 (21) 66 (33) 2 (1) 11 (6)	 1 (1) 2 (2) 0 (0) 0 (0)
Coagulation disorders, n (%) **Total** **von Willebrand Disease** **Type I** **Type II** **Type III** **FXIII deficiency** **FVII deficiency** **FV deficiency** **Hypofibrinogenaemia** **FX deficiency** **FXII deficiency** **Prolonged PFA** **Thrombocytopenia** **No coagulation disorder**	 151 (76)* 118 (59) 113 (57) 5 (3) 0 (0) 15 (8) 9 (5) 6 (3) 2 (1) 1 (1) 2 (1) 15 (8) 7 (4) 48 (24)	 4 (4) 4 (4) 4 (4) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 102 (96)
PBAC-Score	266 (31–4212)	60 (4–100)



Treatment of menorraghia

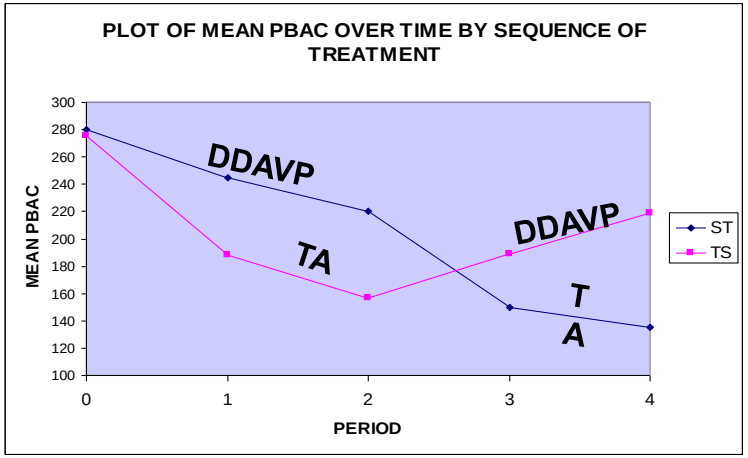
Treatment of acute und chronic menorrhagia

Figure 2



Treatment - Haemostatic

Tranexamic acid and DDAVP (IN spray) - RCT in 116 women







Combination of TA+DDAVP

Improve efficacy
Shorter duration and smaller dose DDAVP
Reduce adverse effects

Edlund 2003

Valette ® und Maxim ®



30µg Ethinylestradiol +
2mg Dienogest



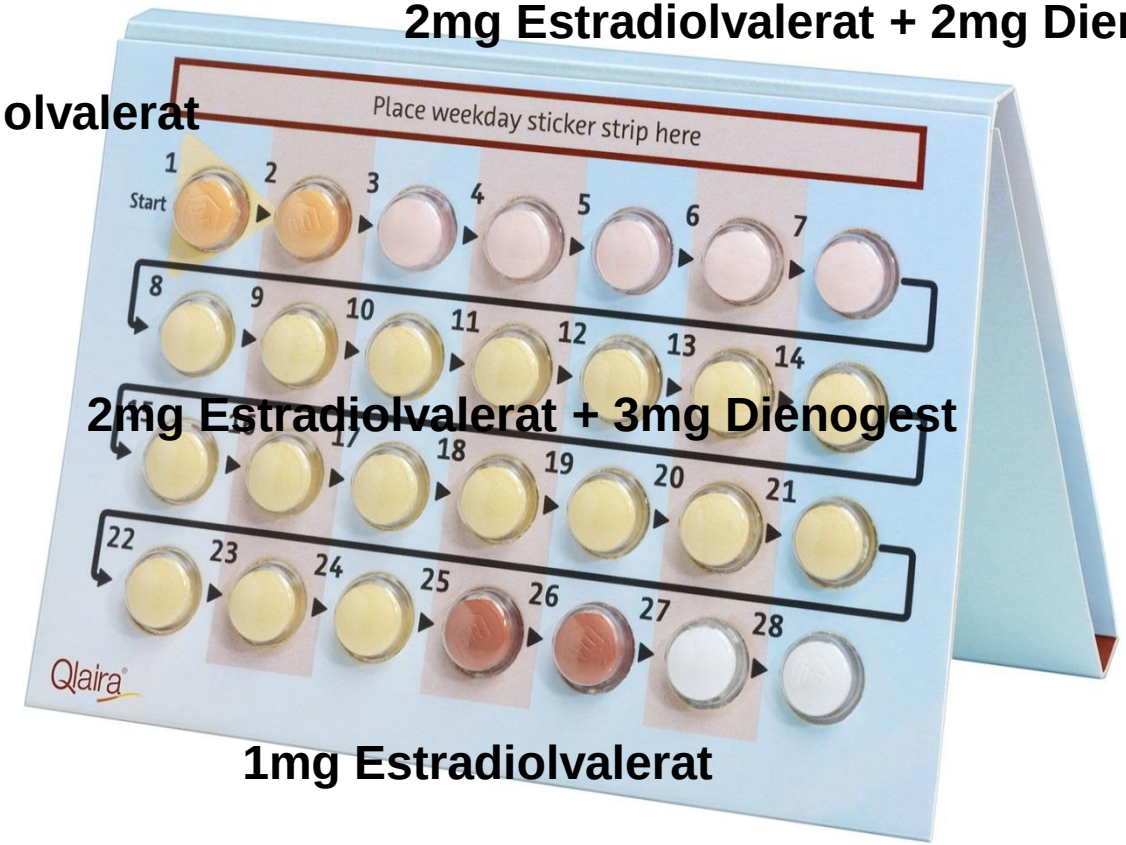
COC pill 4,3,2,1
until the bleed stops

Cave: thrombosis

Qlaira® Wallet

2mg Estradiolvalerat + 2mg Dienogest

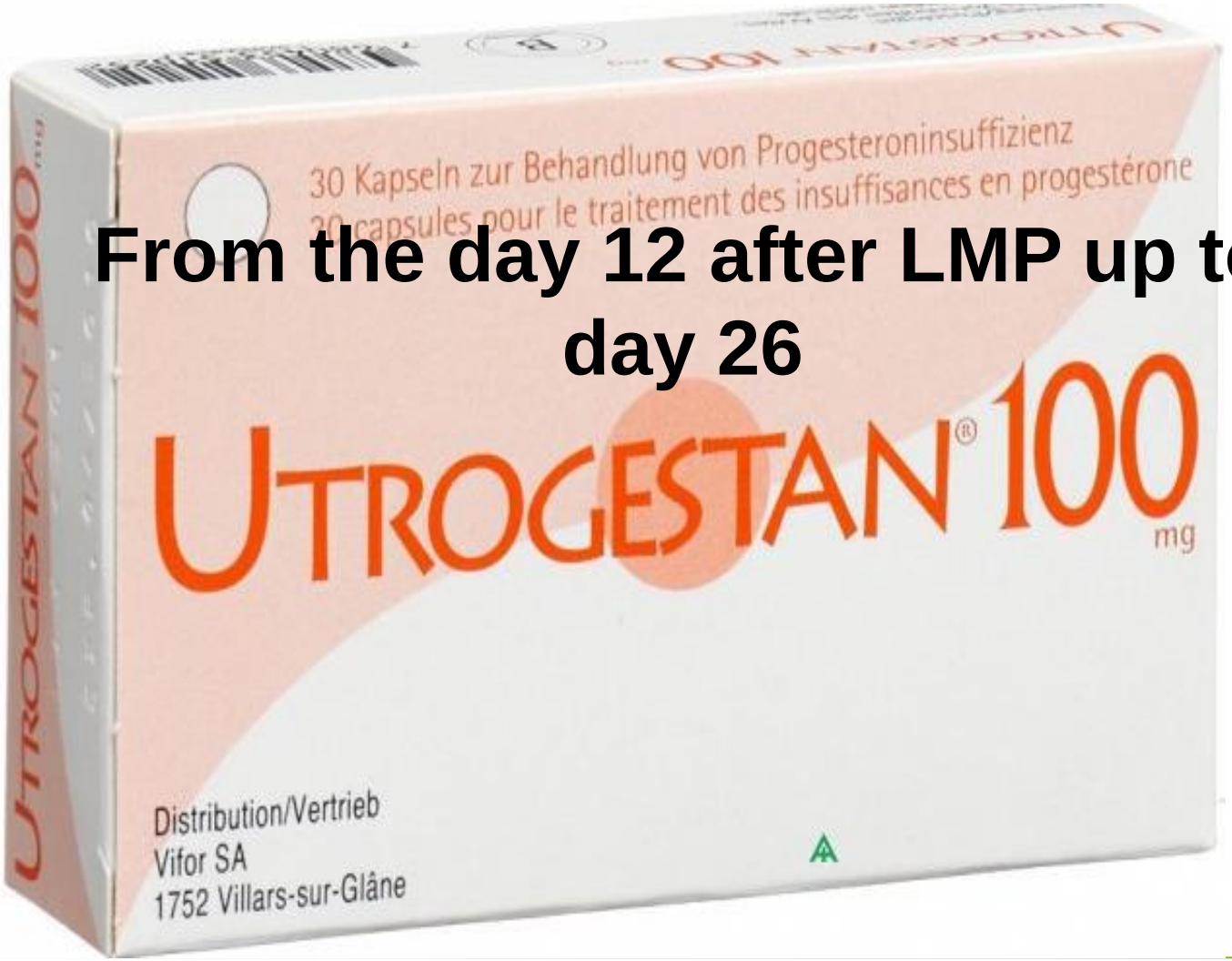
3mg Estradiolvalerat



2mg Estradiolvalerat + 3mg Dienogest

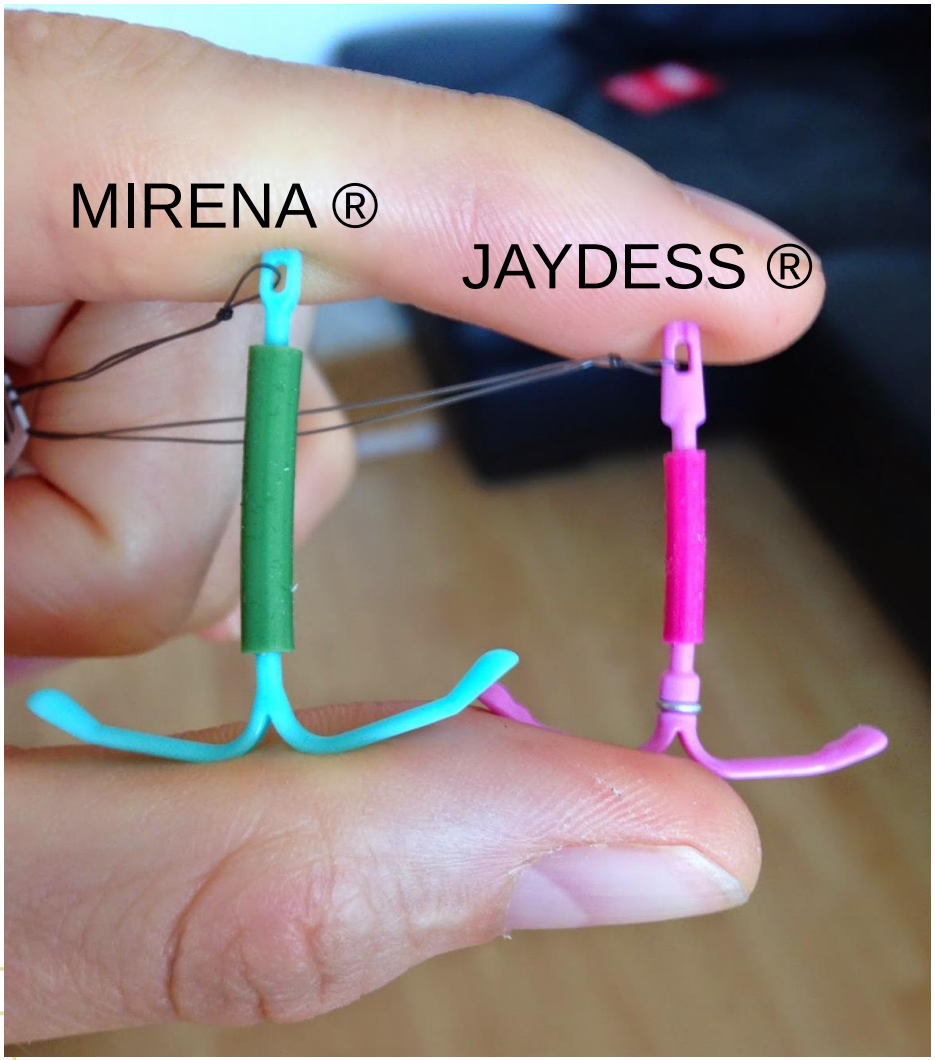
1mg Estradiolvalerat

Utrogestan 100



From the day 12 after LMP up to day 26

LNG-IUS (Mirena- Jaydess)-Women with bleeding disorders



Other Possible Health Benefits

- Most effective reversible contraceptive (5 yr) – (3yr)
- Menstrual pain &PMS
- Endometrial hyperplasia
- Endometriosis, adenomyosis /fibroid

Kingman 2004
Chi, 2010

Take home message

- **To be aware about menorrhagia in adolescence**
- **It is good detectable with the PBAC score**
- **Different ages and situations need different treatment**

dr. rott
dr. halimeh
dr. kappert

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Management of PPH

Dr. med. Susan Halimeh

Definition of PPH

Guidelines	Definition
Australian 2008	Blood loss >500 ml after vaginal delivery and >750 ml following cesarean section
Austrian Guidelines 2008	Blood loss of 500–1000 ml and clinical signs of hypovolemic shock or blood loss >1000 ml
German Guidelines 2008	Blood loss ≥500 ml within 24 hours after birth. Severe PPH is blood loss ≥1000 ml within 24 hours.
RCOG 2009	Primary PPH involving an estimated blood loss of 500–1000 ml (and in the absence of clinical signs of shock) should prompt basic measures (close monitoring, intravenous access, full blood count, group and screen) to facilitate resuscitation should it become necessary. If a woman with primary PPH is continuing to bleed after an estimated blood loss of 1000 ml (or has clinical signs of shock or tachycardia associated with a smaller estimated loss), this should prompt a full protocol of measures to achieve resuscitation and hemostasis.
WHO definition	Blood loss ≥500 ml within 24 hours after birth. Severe PPH is blood loss ≥1000 ml within 24 hours.

approximately 140.000 deaths yearly by **postpartum hemorrhage (PPH)**

Definition of PPH

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Australian 2008	Blood loss >500 ml after vaginal delivery and >750 ml following cesarean section
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WHO definition	Blood loss ≥500 ml within 24 hours after birth. Severe PPH is blood loss ≥1000 ml within 24 hours.

RISK: > 1500 ml

Wise A et al. Curr Opin Anaestiol 2008
McLintock C. Thromb Res 2009

Incidence of maternal mortality

- Causes for the maternal mortality in industrial countries

- **1.Thromboembolism; 2.hypertension, 3.PPH**
- Strong bleeding - 10-15% of all Caesarean sections

- Acute life threatening bleeding: 1:1000 deliveries

INCREASING in industrial contries (1,2% 2008 in England, 1,5% 2009 in France

Gil-Gonzalez D et al. Bull World Health Organ 2006
Sundaram R et al. Anaesthesia 2006
Bonnar J. Baillieres Best Pract Res Clin Obstet Gynaecol 2000
Samanfaya RA et al BJOG 2010
Dupont C et al. IJOA 2009

Reasons for maternal mortality

In Europe 13.4% PPH

Third place for maternal mortality

Khan KS et al. WHO analysis of causes of maternal death:a systematic review. Lancet 2006; 367: 1066-1074

PPH

75- 90% of fetal bleeding are postpartal espesially within the first 4 hours postpartum

Crombach G Gynäkologie 2000
Ramanathan G et al. J. Ostet Gynaecol Can 2006

Risk of PPH after a cesarian
4-times higher than after a spontaneous delivery

Crombach G Gynäkologie 2000

PPH

90% of mortality cases could be avoided

Berg CJ et al. Obstet Gynecol 2005

Risk factors associated with PPH

1. Sociol-demographic factors

- **Age >30 years**
- **Multipara (≥ 5)**- but also PPH by Primipara (OR 5,6)

  Malkiel et al. Isr. Med Assoc J 2008
- **Spanish or asiatic origin**
- **Nicotinabuse**
- **Gestational hypertension**
- **Risk of premature placenta Separation**

Risk factors associated with PPH

2. Gynecological factors

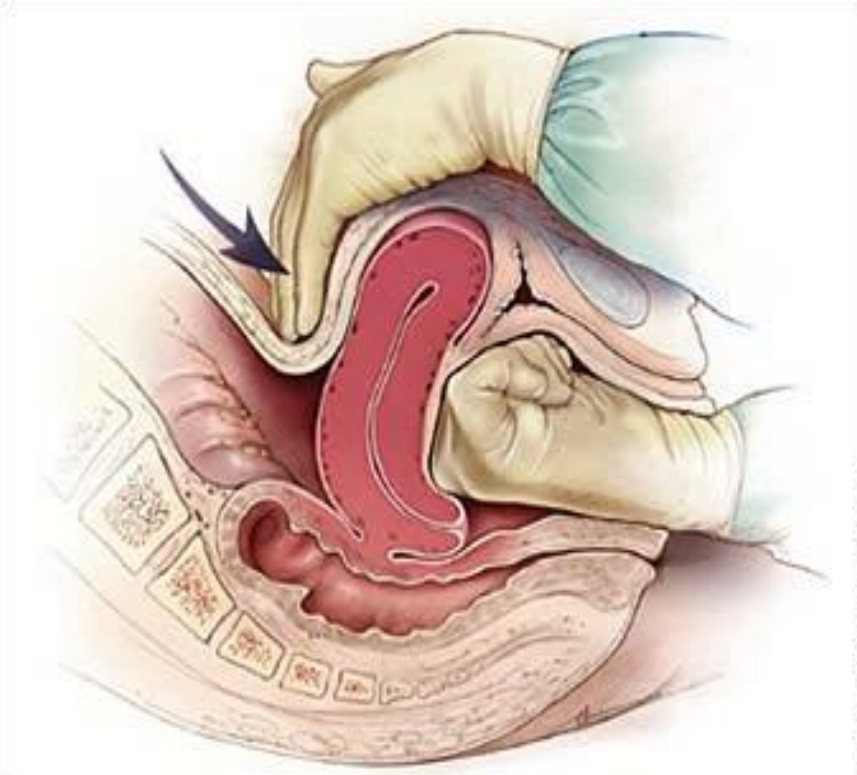
70-80% of PPH

- **Uterine Atony**

80% of all patients with uterine atony show prepartal known riskfactors, only in 20% the bleeding occurs unexpectedely

The uterine atony bleeding are increasing in industrial countries

Knight M et al. BMC 2009



Crombach G Gynäkologie 2000

Risk factors associated with PPH

3. Gynecologic factors

- Abnormal placenta like placenta praevia
- Instrumental interventions like vakuum extraction or forceps
- Myoma
- Uterine enlargement (twins, polyhydramnion, transverse presentation,...)

4. Haematological factors

- Von Willebrand disease
- Carriers of haemophilia A
- Rare bleeding disorders
- Platelet dysfunction

The 4t´s: ***tone*** (postpartale uterine Atony), ***tissue*** (Placental residuals), ***trauma*** **(injury of the birth canal**), ***thrombin*** (coagulopathy)

Haemostais changes during pregnancy

- **Fibrinogen**
- **FVIII**
- **VWF**

} ~ 1.5-3 times
Cave postpartum

- **FVIIa → ~ 2 fach**
- **Thrombomodulin**
- **PAI-1**

- Platelets count
- Fibrinolytic Activity
- Free protein S

Rapid decrease of all factors immediately after birth

No significant variation of FII, FV and FIX

Haemostatic reference intervals in pregnancy

Pal B. Szecsi[1]; Maja Jørgensen[2]; Anna Klajnbard[3]; Malene R. Andersen[1]; Nina P. Colov[3]; Steen Stender[1]

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Summary

Haemostatic reference intervals are generally based on samples from non-pregnant women. Thus, they may not be relevant to pregnant women, a problem that may hinder accurate diagnosis and treatment of haemostatic disorders during pregnancy. In this study, we establish gestational age-specific reference intervals for coagulation tests during normal pregnancy. Eight hundred one women with expected normal pregnancies were included in the study. Of these women, 391 had no complications during pregnancy, vaginal delivery, or postpartum period. Plasma samples were obtained at gestational weeks 13–20, 21–28, 29–34, 35–42, at active labor, and on postpartum days 1 and 2. Reference intervals for each gestational period using only the uncomplicated pregnancies were calculated in all 391 women for activated partial thromboplastin time (aPTT), fibrinogen, fibrin D-dimer, antithrombin, free protein S, and protein C and in a subgroup of 186 women in addition for prothrombin time (PT), Owren and Quick PT, protein S activity, and total protein S and coagulation factors II, V, VII, VIII, IX, X, XI, and XII. The level of coagulation factors II, V, X, XI, XII and antithrombin, protein C, aPTT, PT remained largely unchanged during pregnancy, delivery, and postpartum and were within non-pregnant reference intervals. However, levels of fibrinogen, D-dimer, and coagulation factors VII, VIII, and IX increased markedly. Protein S activity decreased substantially, while free protein S decreased slightly and total protein S was stable. Gestational age-specific reference values are essential for the accurate interpretation of a subset of haemostatic tests during pregnancy, delivery, and puerperium.

Keywords

Fibrin D-dimer, haemostasis, normal pregnancy, protein C, protein S, reference interval

- 801 patients
- 391 patients have no complications
- 186 patients all factors

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Treatment of PPH

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TABLE 4. Recommendations for the prophylactic treatment of women with inherited bleeding disorders*

Deficiency	Management
VWD	
Type 1	TXA, DDAVP
Type 2	TXA, VWF concentrates, DDAVP in responders
Type 3	TXA, VWF concentrates
Afibrinogenemia and hypofibrinogenemia	Replacement therapy according to availability (fibrinogen concentrate, cryoprecipitate, FFP†) and volume status
Dysfibrinogenemia	Women with dysfibrinogenemia are also at risk of both postpartum thrombosis and PPH. Postpartum management of these women should be individualized based on their fibrinogen level as well as personal and family history of bleeding and thrombosis. Postpartum thromboprophylaxis in these patients also requires individualized management.
FII	PCCs to maintain FII level >20%-30%
FV	FFP† (increase FV level to >15%-25%)
FV plus FVIII	FV >15%-25%; FVIII >50% (combination of DDAVP or FVIII concentrate and FFP†)
FVII	rFVIIa or nonactivated plasma-derived FVII concentrate (15-30 μg/kg) for women with FVII level of <10%-20% hemostatic level for uterine bleeding OR surgery may be higher (clinical observation)
FX	Replacement therapy during labor and delivery (FX concentrate or PCC as available) in women with FX levels of <10%-20%. In women with FX level >10%-20% and no significant bleeding history, a conservative approach could be adopted.
FXI	Prophylactic treatment with TXA should be considered after delivery up to 2 weeks. For those with a bleeding phenotype and severe deficiency of FXI should receive FXI concentrate if available, otherwise FFP†. Prophylactic treatment with TXA should be considered after delivery for up to 2 weeks. The concomitant use of TXA and FXI concentrates should be avoided due to increased thrombogenicity
FXIII	The incidence of PPH in women with FXIII deficiency is not known. Successful pregnancy in women with FXIII subunit A deficiency is generally only achieved with replacement therapy throughout pregnancy (using FXIII concentrate); a level >10%-20% during pregnancy should be considered.
Carriers of hemophilia	FVIII carrier: TXA, DDAVP, FVIII replacement (recombinant or plasma derived) F IX carrier: TXA, F IX replacement (recombinant or plasma derived)

* It is possible that a patient may deliver where no products but standard blood products are immediately available for an unexpected bleed. In such cases, FFP is used as a second choice. Cryoprecipitate can also be used as a second choice in carriers of hemophilia, VWD, and fibrinogen and FXIII deficiency. Adapted from Peyvandi et al.,[34] Grade 3-I.

† Virus inactivated when available.

DDAVP = desmopressin; PCC = prothrombin complex concentrate.

TABLE 7. Approaches to prevention and management of PPH

Stage	Patient status	Treatment
Prevention of PPH	Woman with high risk of PPH (Grade 1-I) *(bleeding disorder, placenta previa, twins, antepartum hemorrhage)*	Germany:[35] oxytocin—3 IU bolus IV following cord clamp. Second bolus of 3 IU oxytocin if required France:[56] oxytocin—5 IU IV following cord clamp United Kingdom:[10] oxytocin—5 IU IM (vaginal delivery) or 5 IU IV (cesarean delivery) NB. Some centers have reverted to using Syntometrine after observing an increase in the prevalence of PPH Misoprostol*—800 μg PR TXA (according to national guidelines)
	Woman not at high risk or with no evidence of bleeding (Grade 1-I)	Uterotonic therapy according to country-specific guidelines, e.g., Syntometrine France:[56] oxytocin—5 IU IV following cord clamp, with 10 IU IV infusion (maximum 30 IU in 30 min)
First-line treatment	All women who develop hemorrhage postpartum (Grade 1-I)	Assess clinical response with uterotonic agents (Grade 1-I) IV infusion and IM bolus of oxytocin (combination with prostaglandins considered dependent on local practice†): e.g., Syntocinon (40 IU over 4 hr); ergometrine (500 mg IV): misoprostol (800 μg PR) *Country-specific guidelines:* France:[56] oxytocin infusion (30 IU/30 min) followed by initial Sulprostone infusion (500 μg/1 hr) then 500 μg/6-12 hr depending on the rate of bleeding Germany:[35] oxytocin infusion (10-40 IU oxytocin/500-1000 mL crystalloid solution) depending on uterine tone Persistent bleeding: stop oxytocin infusion. Begin Sulprostone (500 μg/500 mL crystalloid solution) IV 1.7 μg/min (max rate 8.3 μg/min, max dose 1500 μg in 24 hr)
Second-line treatment	Failure to stop bleeding with uterotonics	*Nonsurgical measures:* Coagulation screen TXA (Grade 1-II) Fibrinogen supplementation (Grade 3-I) Blood product transfusion *Obstetric assessment and surgical intervention:* Bimanual compression Balloon tamponade/B-Lynch sutures (the choice depends on the mode of delivery) Packing the uterus Uterine artery embolization
Third-line treatment	Failure to stop bleeding with first operative procedure	B-Lynch sutures if not yet performed Hysterectomy *Nonsurgical:* rFVIIa‡ (Grade 3-I)

* The consensus panel agrees that when considering the benefits safety profile of misoprostol alongside the benefits of its physiologic effects it is reasonable to administer prophylactically in women at high risk of PPH.
† Route of administration and dose varies between countries.
‡ Administration is off-label and the group did not reach consensus regarding its role in management of PPH.
IU = international unit; IM = intramuscular; PR = per rectal; U = unit.

ORIGINAL ARTICLE

Evaluation and management of postpartum hemorrhage: consensus from an international expert panel

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Transfusion Nov. 2013

Recommended treatment algorithm for the treatment of PPH

Steps 1 and 2 should occur in parallel

Postpartum blood loss >500mL – PPH declared

1. Fundal massage
2. Establish IV access
3. Uterotonic therapy
4. Take bloods for CBC, APTT, PT ratio, Fibrinogen, and group and screen (or crossmatch)

→ Initial treatment successful & Bleeding controlled → Close observation CBC at 12 and 24 hours

Initial treatment unsuccessful – persistent (ongoing) PPH >1000mL

Ongoing, uncontrollable PPH >2000mL

1. Immediate resuscitation AND 2. Identify and treat cause

Further escalation

Maintain circulating blood volume and tissue oxygenation

Management of obstetric causes of bleeding: uterine atony, retained products of conception and genital tract trauma

1. Send to operating room for obstretic assessment
2. Continue massage and uterotonics
3. Uterine tamponade: bimanual compression, uterine balloon (vaginal delivery)
4. Repair tears, lacerations
5. Placenta not deliverable? (consider placenta accreta

1. Uterine brace sutures (if not yet performed)
2. Uterine artery embolization
3. Uterine artery ligation if no facility for UAE or patient too unstable for transfer for UAE
4. Internal iliac artery ligation (only in the presence of surgical expertise) and usually as an addition to uterine tamponade
5. Hysterectomy (as last resort)

Correction of coagulopathy

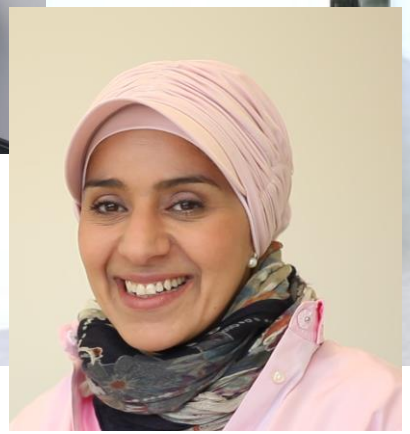
1. Coagulation screen (platelets, APTT, PT ratio, fibrinogen Results, TEG, ROTEM)Continue assessment of coagulation every 45 – 60 mins Until PPH is controlled
2. TXA 1g IV, repeat after 30 mins
3. Blood and plasma product replacement (consider early fibrinogen replacement

1. Trigger massive transfusion protocol
2. Correct hypotermia, acidosis, Hypocalcemia
3. Consider rFVIIa before hysterectomy



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Thank you for your attention

Gracias por su atención