Съезд Congress

5-7 сентября 2018 / Санкт-Петербург
September 5-7, 2018 / St. Petersburg

Prof. Alexander Ioscovich

Director of Obstetric and Ambulatory Anesthesia Department,
Shaare Zedek Medical Center, Hebrew University, Jerusalem

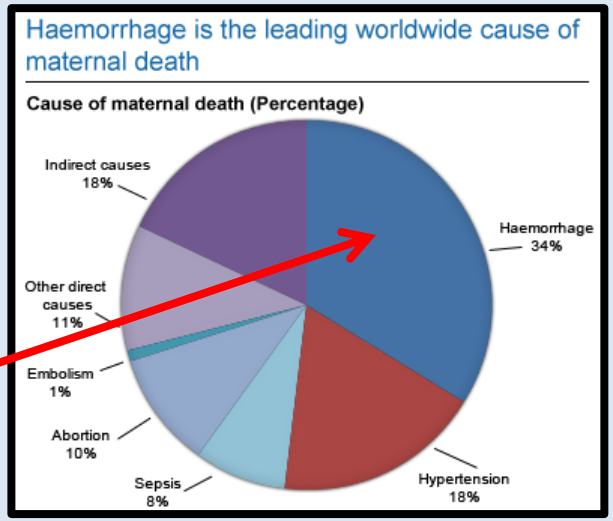
Massive Obstetric Hemorrhage: Anesthetic point of view

Shaare Zedek Medical Center, Jerusalem

16.000+6.000 labors annually

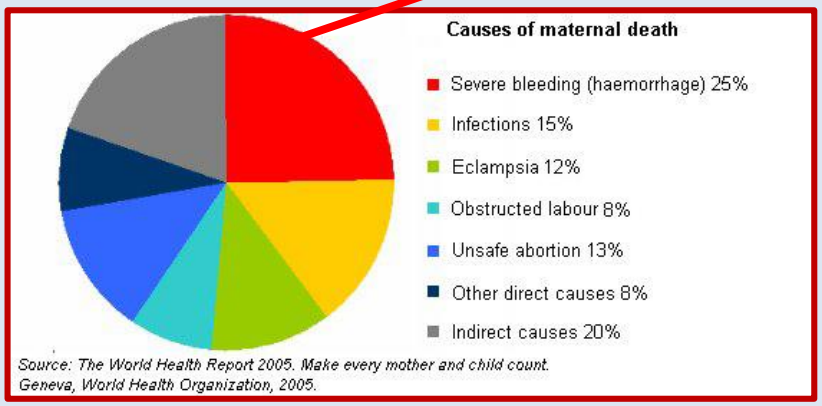
12% of caesarean sections
53-55% of epidural analgesia

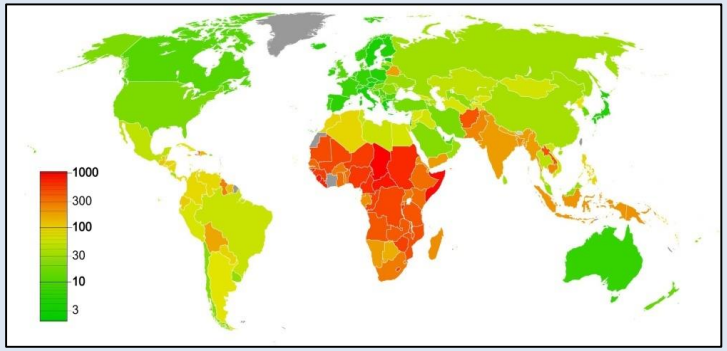
The most recent Practice Bulletin from the
American College of Obstetricians and Gynecologists
places the estimate at 140,000 maternal deaths
per year or 1 woman every 4 minutes.



Source: WHO, Systematic Review of Causes of Maternal Death , 2010

Reference: http://www.childinfo.org/maternal_mortality.html





Post Partum Haemorrhage **(PPH)**- Causes and Risk Factors

TABLE 3. Risk factors associated with PPH

Category and risk factor	OR or range >500 mL EBL	OR or range >1000 mL EBL
Sociodemographic		
Asian ethnicity[12]	1.8-2	
Hispanic ethnicity[15]	1.7	
Age ≥ 30 years[12,16]	1.3-1.4	1.5
Obstetric		
Prolonged Stage 3 labor[15]	7.6	
Preeclampsia[15]	5.0	
Retained placenta[11,13,18,19]	4.1-7.8	11.7-16.0
Known placenta previa[17,19]	4-13.1	15.9
Previous PPH[15]	3.0-3.6	
Suspected or proven placental abruption[17,19]	2.9-12.6	2.6
Multiple gestation[12,20,21]	2.3-4.5	2.6
Fetal macrosomia[12,18,19]	1.9-2.4	
HELLP syndrome[12]	1.9	
Polyhydramnios[11]	1.9	
Oxytocin exposure[14]	1.8	
Induction of labor[12,18,19]	1.3-2	2.1-2.4
Prolonged labor[12,15]	1.1-2	
Surgical		
Emergency cesarean delivery[12]	3.6	
Elective cesarean delivery[12]	2.5	
Forceps delivery[12]	1.9	
Vacuum delivery[12]	1.8	
Episiotomy[15,18,19]	1.7-4.5	
Perineal suture[18]	1.7	2.5
Systemic or medical		
Antepartum hemorrhage[11]	3.8	
VWD[12]	3.3	
Anemia (<9 g/dL)[12]	2.2	
Pyrexia in labor[10]	2	
Obesity (BMI > 35)[19]	1.6	
Cardiac disease[12]	1.5	

BMI = body mass index; EBL = estimated blood loss.

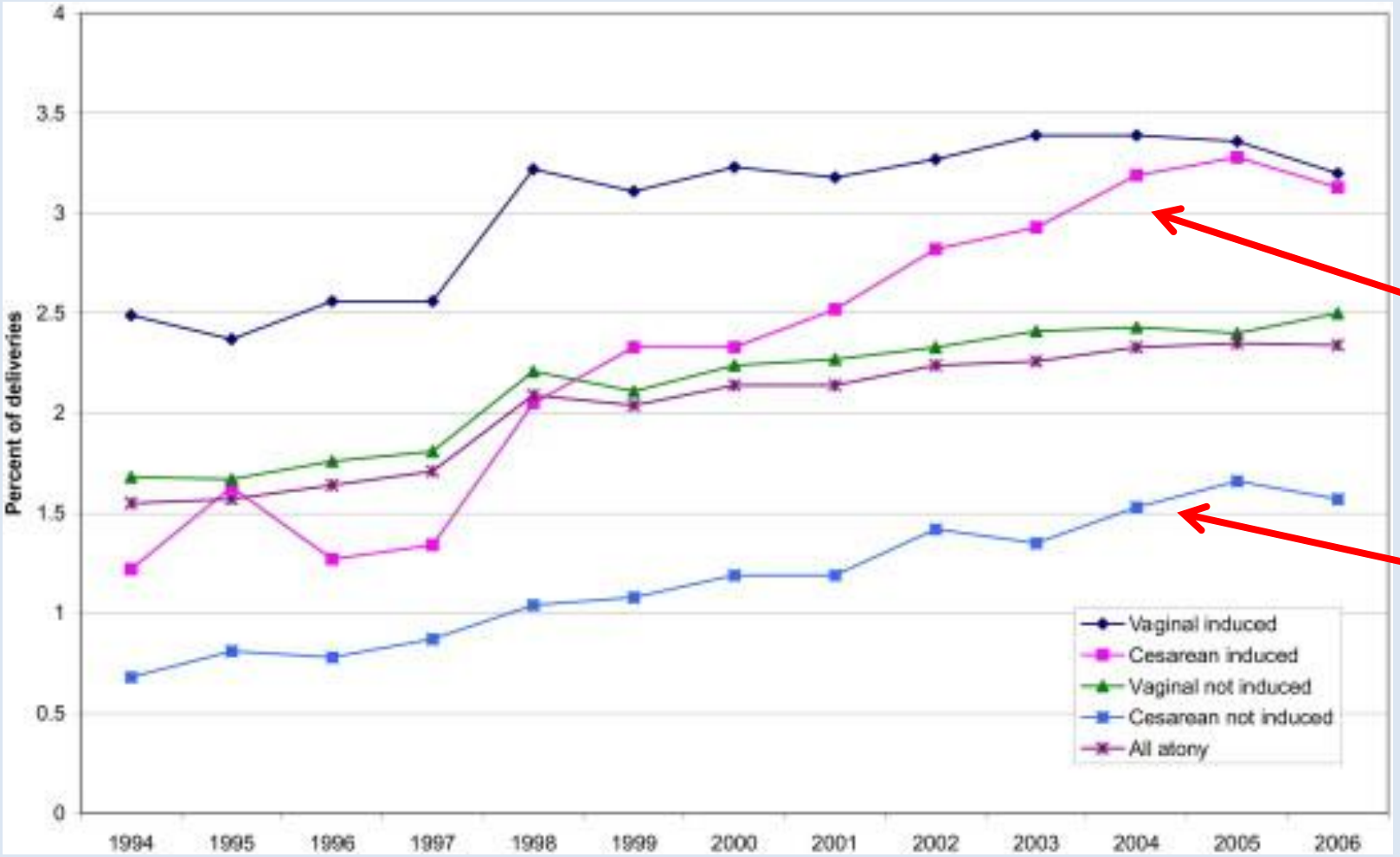
The causes of PPH can be classified into four main groups

- **Uterine atony (up to 80%)**
- **Placental problem**
- **Genital tract trauma**
- **Systemic medical disorders**

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

Rezan Abdul-Kadir,[1] Claire McLintock,[2] Anne-Sophie Ducloy,[3] Hazem El-Refaey,[4] Adrian England,[5] Augusto B. Federici,[6] Chad A. Grotegut,[7] Susan Halimeh,[8] Jay H. Herman,[9] Stefan Hofer,[10] Andra H. James,[11] Peter A. Kouides,[12] Michael J. Paidas,[13] Flora Peyvandi,[14] and Rochelle Winikoff[15]

TRANSFUSION 2014;54:1756-1768.



Trends in peripartum hemorrhage: United States, 1994–2006

American Journal of Obstetrics and Gynecology
Volume 202, Issue 4, April 2010, Pages 353.e1–353.e6

Definition of PPH (up to 4-5 %)

TABLE 2. Summary of primary PPH definitions in current use globally[7-10]

Guidelines	Definition
Australian 2008	Blood loss of >500 mL after vaginal delivery and >750 mL after 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 of ≥500 mL within 24 hr after birth Severe PPH is blood loss of ≥1000 mL within 24 hr
UK Royal College of Obstetricians and Gynaecologists 2009	Primary PPH—estimated blood loss of 500-1000 mL in the absence of clinical signs of shock Severe PPH—estimated blood loss of >1000 mL or clinical signs of shock or tachycardia with a smaller estimated loss
WHO definition	Blood loss of ≥500 mL within 24 hr after birth Severe PPH is blood loss of ≥1000 mL within 24 hr

"Persistent (ongoing) PPH is active bleeding >1000 mL within the 24 hours following birth that continues despite the use of initial measures including first-line uterotonic agents and uterine massage."

Definition of Major PPH

Moderate
1000-2000mL

Severe
>2000mL

Massive PPH (> 2500mL) 5-6 per 1000

- **Fall in Hemoglobin concentration of ≥4 mg/dL**
- **The need for the transfusion of > 4 units of red cells (PC)**
- **Development of Coagulopathy**
- **The need for an invasive procedure : embolisation, hysterectomy…**

Lennox C, Marr L. Scottish Confidential Audit of Severe Maternal Morbidity. 9th Annual Report (data from 2011). http://healthcareimprovementscotland.org/his/idoc.ashx?docid=5fb640e2-d079-48cc-ad49-a58f6929b685&version=-1 (accessed 17/09/2014).

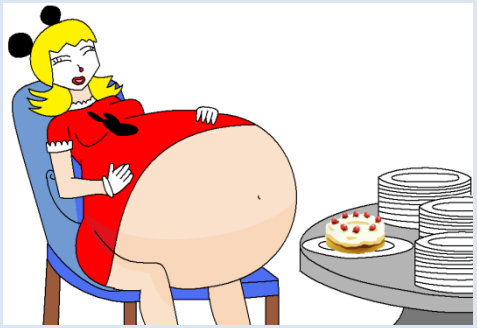
MEDICAL INTELLIGENCE ARTICLE

Medical Advances in the Treatment of Postpartum Hemorrhage

(Anesth Analg 2014;119:1140–7)

Anne-Sophie Ducloy-Bouthors, MD,* Sophie Susen, MD, PhD,†‡ Cynthia A. Wong, MD,§
Alex Butwick, MBBS, FRCA, MS,‖ Benoit Vallet, MD, PhD,* and Evelyn Lockhart, MD¶

- **Rapid laboratory Monitoring** of coagulopathy in the setting of PPH
- **Modern approach to transfusion therapy**
- **Prohemostatic pharmacotherapy** as an adjunct to transfusion



Pregnant women are not a women with big belly

Massive PPH ≠ Massive trauma-associated hemorrhage

Trauma patient differ from obstetric patient:

- They are primarily male
- Mechanisms of trauma and obstetric hemorrhage are difference
- They hemostatic physiology is different

Szecsi PB, Jørgensen M, Klajnbard A, Andersen MR, Colov NP, Stender S. Haemostatic reference intervals in pregnancy. Thromb Haemost 2010;103:718–27

Changes in the hemostasis at term

- Prothrombotic (Hypercoagulable) state
- Levels of ALL procoagulant factors (except factor XI) increased
  - Fibrinogen and factor VIII ↑ up to 100-150% (4-6g/L)
  - Von Willebrand factor ↑ up to 300%
  - Shorter PT/aPTT
  - D-dimer level increase
  - Increase in TEG parameters
- Natural anticoagulants (protein C and S) fall
  - Increase in fibrinolysis
- Gestational thrombocytopenia

Allard S, Green L, Hunt BJ. How we manage the haematological aspects of major obstetric haemorrhage. *British Journal of Haematology* 2014; **164**: 177–88.

Thachil J, Toh CH. Disseminated intravascular coagulation in obstetric disorders and its acute haematological management. *Blood Reviews* 2009; **23**: 167–76.

O'Riordan MN, Higgins JR. Haemostasis in normal and abnormal pregnancy. *Best Practice and Research. Clinical Obstetrics and Gynaecology* 2003; **17**: 385–96.

Liu X, Jiang Y, Shi H, Yue X, Wang Y, Yang H. Prospective, sequential, longitudinal study of coagulation changes during pregnancy in Chinese women. *International Journal of Gynecology and Obstetrics* 2009; **105**: 240–3.

Szecsi PB, Jorgensen M, Klajnbard A, Andersen MR, Colov NP, Stender S. Haemostatic reference intervals in pregnancy. *Thrombosis and Haemostasis* 2010; **103**: 718–27.

Measurement of blood loss during postpartum haemorrhage

G. Lilley,[a] D. Burkett-st-Laurent,[a] E. Precious,[b] D. Bruynseels,[a] A. Kaye,[c] J. Sanders,[c,d] R. Alikhan,[b] P.W. Collins,[b,e] J.E. Hall,[a,e] R.E. Collis[a]

[a]*Department of Anaesthetics and Pain Control,* [b]*Department of Haematology,* [c]*Department of Obstetrics, Cardiff and Vale University Health Board, UK,* [d]*Institute of Translation, Innovation, Methodology and Engagement, South East Wales Trials Unit,* [e]*Institute of Infection and Immunity, Critical Illness Research Group, Cardiff University School of Medicine, UK*

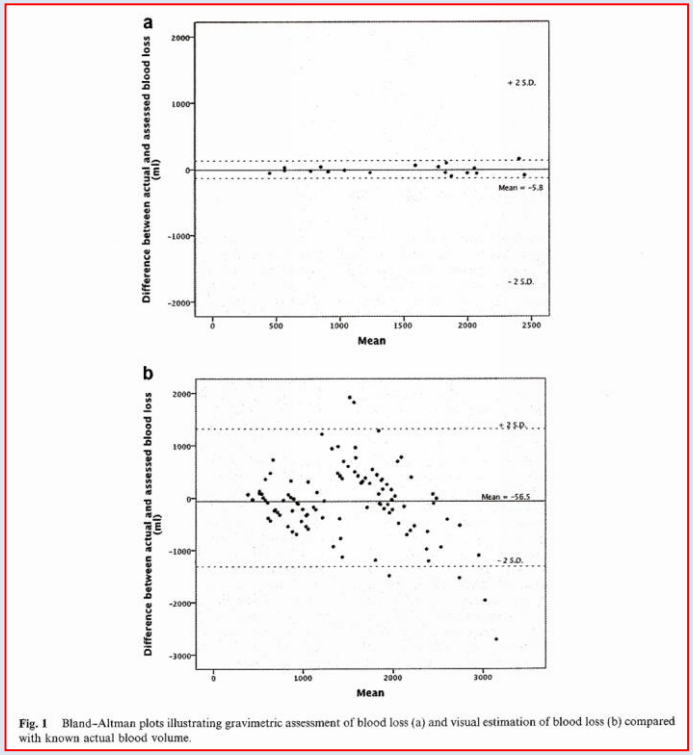


Fig. 1 Bland–Altman plots illustrating gravimetric assessment of blood loss (a) and visual estimation of blood loss (b) compared with known actual blood volume.

- **Blood loss often estimated visually**
- **Underestimation of 30-50% for large volumes**

Lilley G et al. IJOA Feb 2015;24:8-14

Methods of Blood Loss Estimation

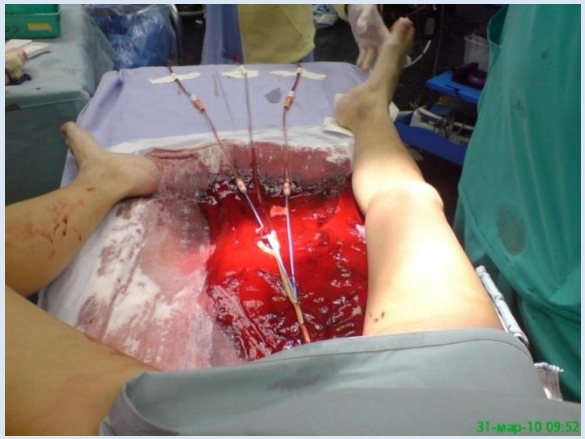
- Visual assessment
- Direct collection of blood
- Gravimetric
- Determination of Hg changes

Failures of each method

- Acidhematin method (spectrophoto lisis)
- Plasma volume changes (radioactive traced ments)
- Measurement of Cr-tagged erythrocytes

Underestimation of perioperative/ peripartum bleeding!!!

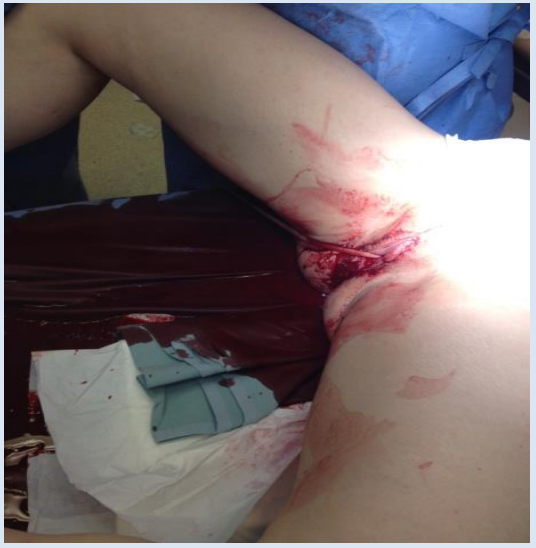
Estimated Blood Loss in PPH



3.2 kg

~1 kg

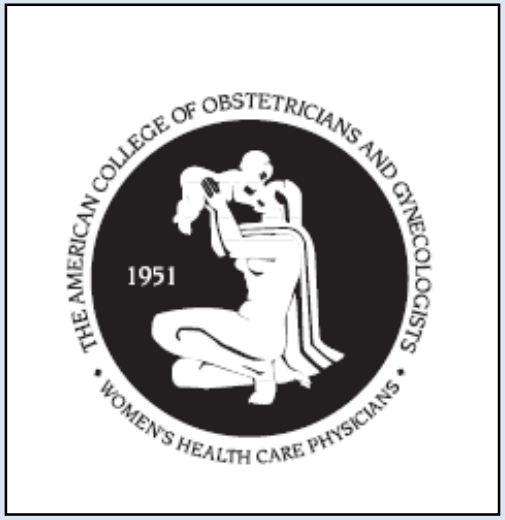
1.2 kg



Reason and Rate of Transfusion of Blood Products

The decision to perform blood transfusion should be made on both

- **Clinical and**
- **Hematological grounds**



Monitoring (Laboratory diagnosis)

- **"Classical"** - laboratory-based method
  - PT/aPTT; Fibrinogen; PLT; Hgb
- **"Modern"** - Point-of-care testing
  - **Tromboelastography** (**TEG**; Haemonetics; USA)
  - **Tromboelastometry** (**ROTEM**; TEM GmBH; Germany)
  - **Continues total hemoglobin monitoring** Masimo
- Clinical observation with empirical blood product replacement

PT/aPTT

- ***During PPH PT/aPTT remain normal despite large amounts of bleeding.***
  - In a cohort of 456 women with PPH, most had normal PT/aPTT until blood loss reached 5000mL.

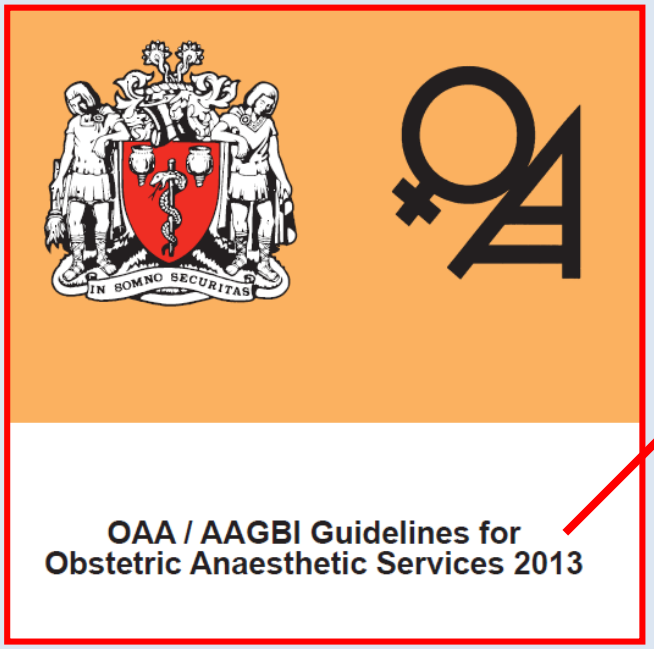
De Lloyd L, Bovington R, Kaye A, et al. Standard haemostatic tests following major obstetric haemorrhage. *International Journal of Obstetric Anesthesia* 2011; **20**: 135–41.

Fibrinogen is an important predictor of severity of PPH

- Fibrinogen concentration < 2g/L compared with fibrinogen concentration >3g/L was
  - Predictive of severe PPH with positive pred.value of 100%
  - Specificity of severe PPH was 99.3%

Gayat E, Resche-Rigon M, Morel O, Rossignol M, Mantz J, Nicolas-Robin A, Nathan-Denizot N, Lefrant JY, Mercier FJ, Samain E, Fargeaudou Y, Barranger E, Laisné MJ, Bréchat PH, Luton D, Ouanounou I, Plaza PA, Broche C, Payen D, Mebazaa A. Predictive factors of advanced interventional procedures in a multicentre severe postpartum haemorrhage study. Intensive Care Med 2011;37:1816–25

Cortet M, Deneux-Tharaux C, Dupont C, Colin C, Rudigoz RC, Bouvier-Colle MH, Huissoud C. Association between fibrinogen level and severity of postpartum haemorrhage: secondary analysis of a prospective trial. Br J Anaesth 2012;108:984–9



- ***Rapid hematological analysis*** *(TEG;ROTEM) as an important support service and* ***"strongly recommended"*** *the availability of bedside estimation of coagulation status and for early diagnosis of hypofibrinogenemia.*

PPH –induced hypofibrinemia was identified by the decrease in FIBTEM (a ROTEM reflecting fibrinogen concentration to clot strength) amplitude. With 100% sensitivity and 85% specificity to detect fibrinogen concentration in PPH >1.5 L.
Huissound C. 2009

International Journal of Obstetric Anesthesia (2014) 23, 10–17
0959-289X/$ - see front matter
http://dx.doi.org/10.1016/j.ijoa.2013.07.003

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ORIGINAL ARTICLE

Major obstetric haemorrhage: monitoring with thromboelastography, laboratory analyses or both?

O. Karlsson,[a] A. Jeppsson,[b] M. Hellgren[c]
[a] *Department of Anaesthesiology, Sahlgrenska University Hospital, Gothenburg, Sweden*
[b] *Department of Cardiovascular Surgery and Anaesthesia, Sahlgrenska University Hospital and Department of Molecular and Clinical Medicine, University of Gothenburg, Gothenburg, Sweden*
[c] *Department of Obstetrics, Sahlgrenska University Hospital, Gothenburg and Department of Prenatal Care, Primary Care, South Bohuslän, Sweden*

Table 3 Thromboelastography variables

	Controls ($n = 49$)	MOH all ($n = 45$)	MOH 2–3L ($n = 35$)	MOH > 3L ($n = 10$)
R (min)	6.3 (5.8 to 6.9) [1.8–13.4]	5.1† (4.5 to 5.7) [1.3–9.6]	5.2 (4.5 to 5.9) [1.6–9.6]	4.5 (3.2 to 5.9) [1.3–6.7]
K (min)	1.8 (1.6 to 2.1) [1.0–5.3]	2.0 (1.8 to 2.2) [1.2–3.7]	2.0 (1.8 to 2.2) [1.2–3.7]	2.1 (1.6 to 2.6) [1.3–3.3]
Angle (degree)	65.2 (62.7 to 67.6) [38.6–77.1]	61.3* (58.7 to 63.8) [42.1–72.1]	61.4 (58.4 to 64.3) [42.1–72.1]	60.8 (55.0 to 66.7) [48.5–71.8]
MA (mm)	72.9 (71.4 to 74.4) [54.2–81.6]	64.8Σ (62.4 to 67.3) [38.0–79.4]	65.1 (62.2 to 68.1) [38.0–79.4]	63.8 (59.7 to 67.9) [55.4–74.6]
LY30 (%)	1.5 (0.9 to 2.2) [0–9.3]	0.4 † (0.1 to 0.7) [0–5.9]	0.4 (0.1 to 0.8) [0–5.9]	0.2 (−0.06 to 0.4) [0–0.9]

Data are mean, (95% CI) and [range]. R: time to start of clotting; K: time to 20 min clot firmness; Angle: clot growth rate; MA: maximum clot amplitude; LY30: lysis 30 min after maximum amplitude. * $P < 0.05$; † $P < 0.01$; Σ $P < 0.0001$ compared to controls.

Point-of-care testing of coagulation and fibrinolytic status during postpartum haemorrhage: developing at

thrombelastography®-guided transfusion algorithm.

Hill JS, Devenie G, Powell M. New Zealand Anaesth Intensive Care. 2012 Nov;40(6):1007-15.

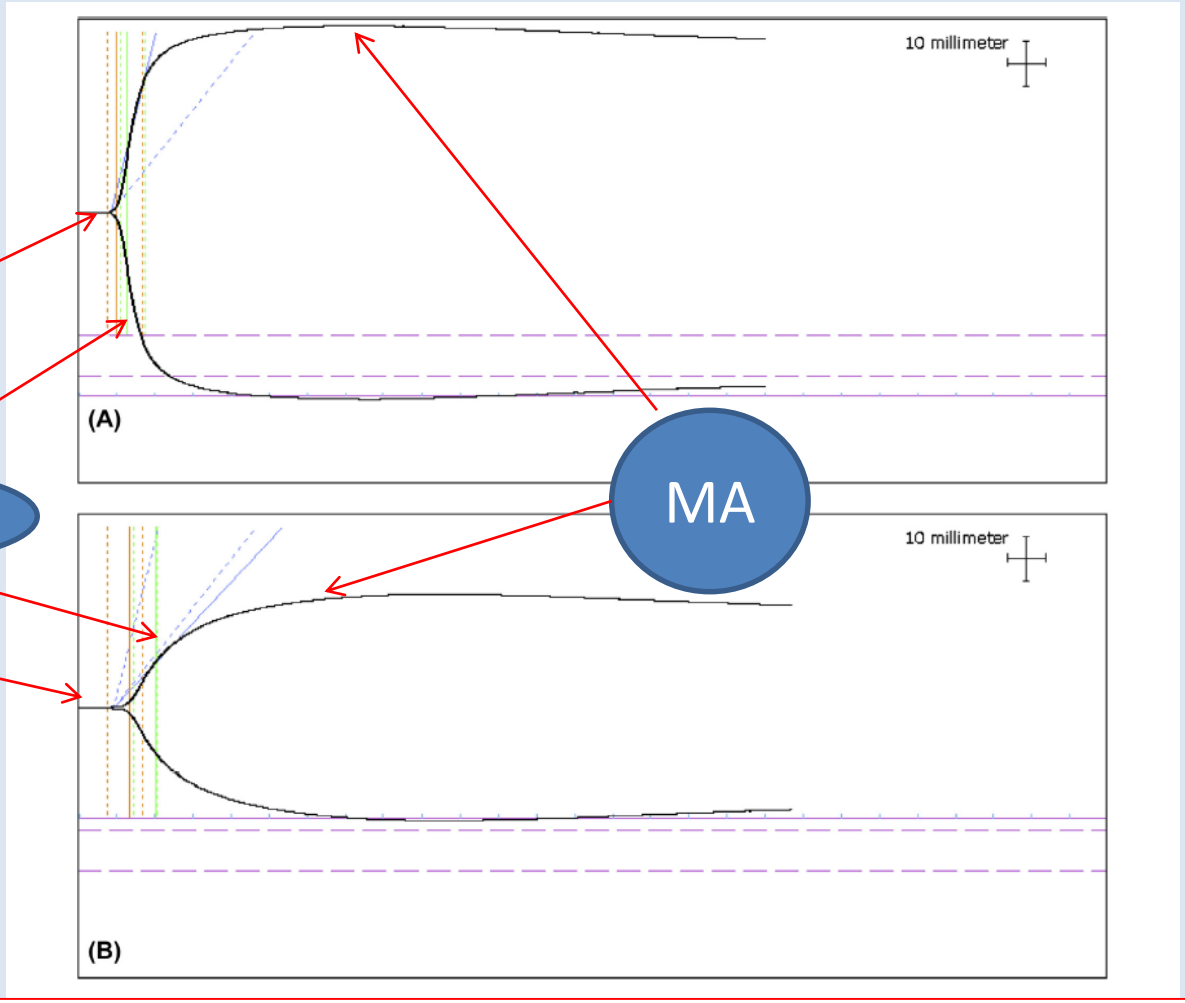
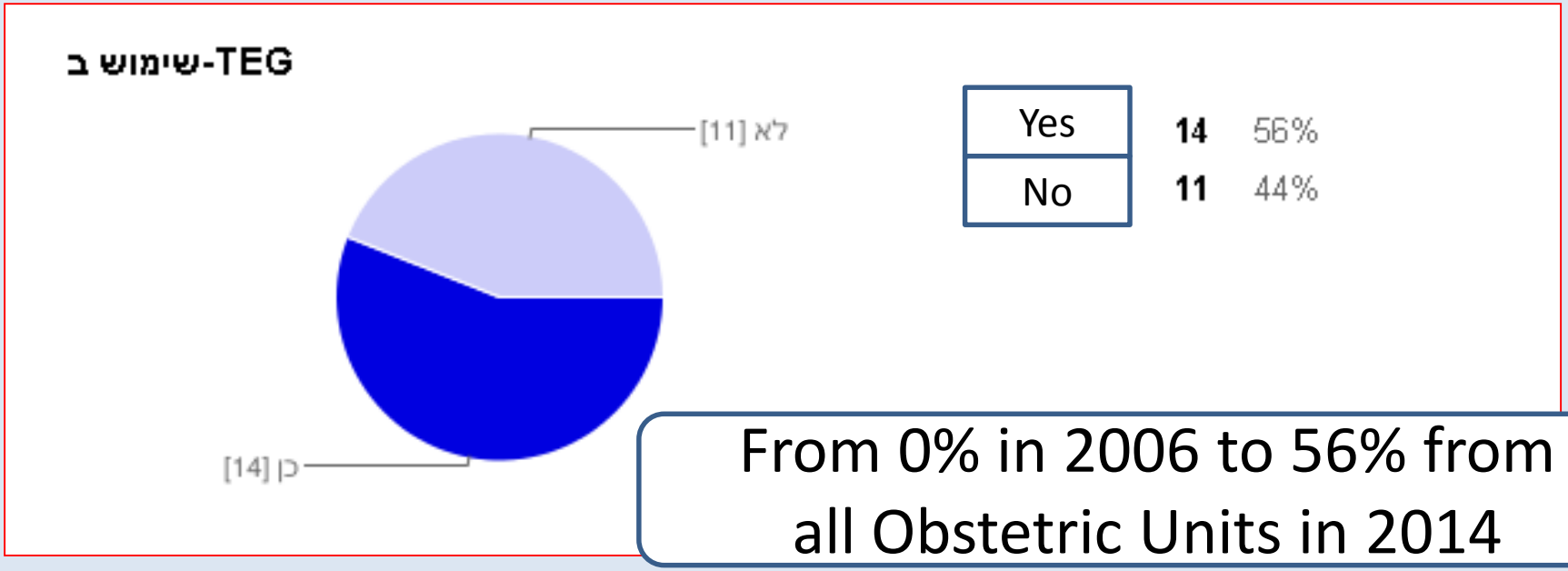


Fig. 1 Two thromboelastographic profiles. (A) TEG profile in a woman with normal bleeding postpartum. Estimated blood loss 250 mL, TEG-R 4.9 min, TEG-MA 81.4 mm, platelets 239×10^9/L, fibrinogen 6.0 g/L and antithrombin 0.98 kIU/L. (B) TEG profile in a woman with major obstetric haemorrhage. Estimated blood loss 2500 mL, TEG-R 6.6 min, TEG-MA 48.9 mm, platelets 55×10^9/L, fibrinogen 1.7 g/L, antithrombin 0.37 kIU/L.

Turnaround time PT/aPTT - TEG from 35±37min to 14±3 min

Chandler WL, Ferrell C, Trimble S, Moody S. Development of a rapid emergency hemorrhage panel. Transfusion 2010;50:2547–52
Chandler WL. Emergency assessment of hemostasis in the bleeding patient. Int J Lab Hematol 2013;35:339–43

TEG for Massive bleeding in CS in Israel



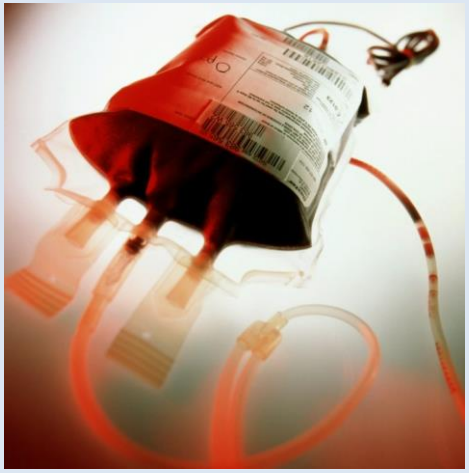
From 0% in 2006 to 56% from all Obstetric Units in 2014

Acta Anaesthesiologica Scandinavica
AN INTERNATIONAL JOURNAL OF ANAESTHESIOLOGY AND INTENSIVE CARE, PAIN AND EMERGENCY MEDICINE

Israeli survey of anesthesia practice related to placenta previa and accreta

A. Ioscovich[1,*], D. Shatalin[1,*], A. J. Butwick[2], Y. Ginosar[3], S. Orbach-Zinger[4] and C. F. Weiniger[3]

- Loss of 30–40% of CBV (around 1500–2000 mL) – hypovolemia by crystalloids and synthetic colloids must be corrected urgently, and red cell transfusion is usually indicated;
- Loss of >40% of CBV (>2000 mL) – urgent correction of hypovolemia, including red cell transfusion, must be performed (2, 4, 9, 23).



There are no firm criteria for initiating red cell transfusion.

Target level of Hb

- Hb <6 g/dL, transfusion almost always indicated;
- Hb 6–10 g/dL, indication for transfusion is based individually for every patient and should be motivated (1, 2, 4, 9, 24).

When Hb level is ≤7 g/dL and anemia is asymptomatic, transfusion is needed if massive bleeding is expected during surgery or the patient belongs to a high anesthetic risk group (4).

Next step in the "Point of Care" of massive bleeding is Total hemoglobin

(SpHb®)–noninvasive continuous monitoring

Results

A total of 32 studies (4425 subjects, median sample size of 44, ranged from 10 to 569 patients per study) were included in this meta-analysis. The overall pooled random-effects mean difference (noninvasive-central laboratory) and SD were 0.10 ± 1.37 g/dL (-2.59 to 2.80 g/dL, I = 95.9% for mean difference and 95.0% for SD). In subgroup analysis, pooled mean difference and SD were 0.39 ± 1.32 g/dL (-2.21 to 2.98 g/dL, I = 93.0%, 71.4%) in 13 studies conducted in the perioperative setting and were -0.51±1.59 g/dL (-3.63 to 2.62 g/dL, I = 83.7%, 96.4%) in 5 studies performed in the intensive care unit setting.

Conclusions

Although the mean difference between noninvasive Hb and central laboratory measurements was small, the wide limits of agreement mean clinicians should be cautious when making clinical decisions based on these devices.

Accuracy of Continuous Noninvasive Hemoglobin Monitoring: A Systematic Review and Meta-Analysis

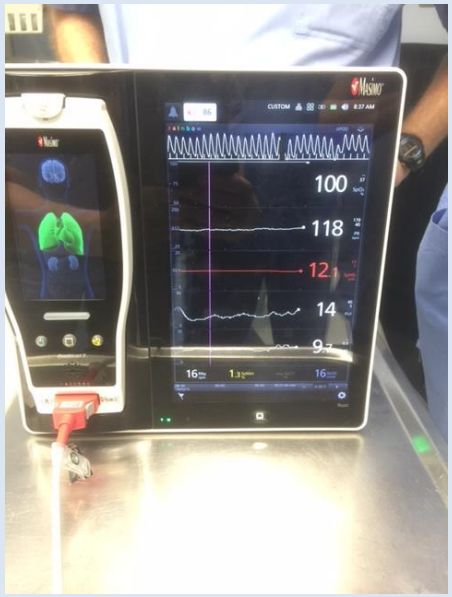
Kim S.H., Lilot M., Murphy L.S., Sidhu K.S., Yu Z., Rinehart J., Cannesson M. *Anesth Analg.* 2014 Jun 9.

Noninvasive and Continuous Trending of Hemoglobin during Labor and in the Post-Partum Period

Tola G., Capogna G. *Euroanesthesia 2014:* Abstract 11AP3-1.

Conclusion

SpHb was able to detect changes in hemoglobin concentration during and after delivery and therefore may provide a means for the early detection of bleeding and postpartum hemorrhage.



~0.3-0.6 ± SD ~1g/dL

- 11.7g/dL - **(SpHb®)** 12.9g/dL
- 11.1g/dL - **(SpHb®)** 11.8g/dL

- 11.2 g/dL - **(SpHb®)** 11.3 g/dL
- 11.8 g/dL - **(SpHb®)** 11.6 g/dL

THE OPEN MIND

XXX 2015 • Volume XXX • Number XXX www.anesthesia-analgesia.org

OPEN

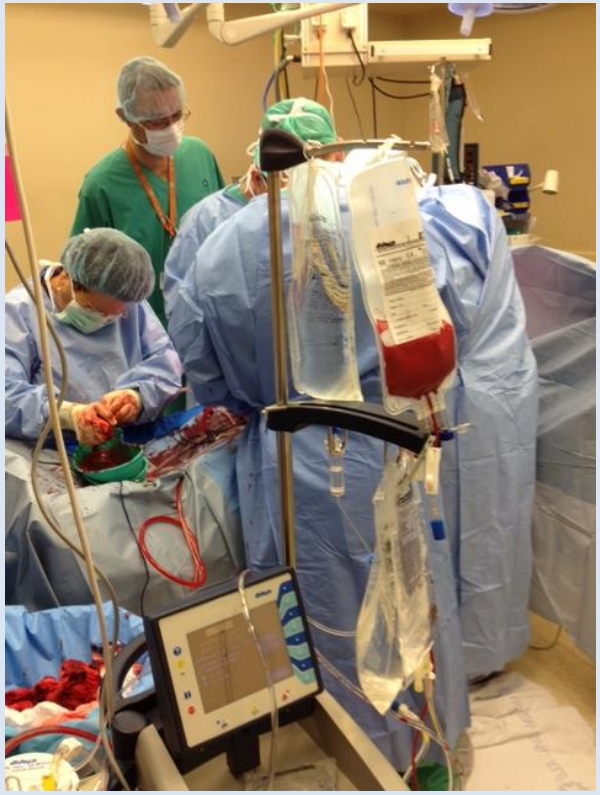
Continuous Noninvasive Hemoglobin Monitoring: A Measured Response to a Critical Review

Steven J. Barker, PhD, MD,* Aryeh Shander, MD,†‡ and Michael A. Ramsay, MD§

AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

ACOG committee opinion.
Placenta accreta. Number 266, January 2002.

Cell saver technology should be considered if available as well as the appropriate location and timing for delivery to allow access to adequate surgical personnel and equipment.



Facilities for blood salvage (cell saver technique) must be available in every obstetric theatre.
Thomas D. and Clark V.
Int J Obstet Anesth. 2005 Jan;14(1):48-50. 50-52

Issue date: November 2005

NHS
National Institute for Health and Clinical Excellence

Intraoperative blood cell salvage in obstetrics

Cost-effectiveness Analysis of Intraoperative Cell Salvage for Obstetric Hemorrhage.
Lim G, et al. Anesthesiology. 2018.

CONCLUSIONS: The use of cell salvage for cases at high risk for obstetric hemorrhage is economically reasonable; routine cell salvage use for all cesarean deliveries is not. These findings can inform the development of public policies such as guidelines on management of obstetric hemorrhage.

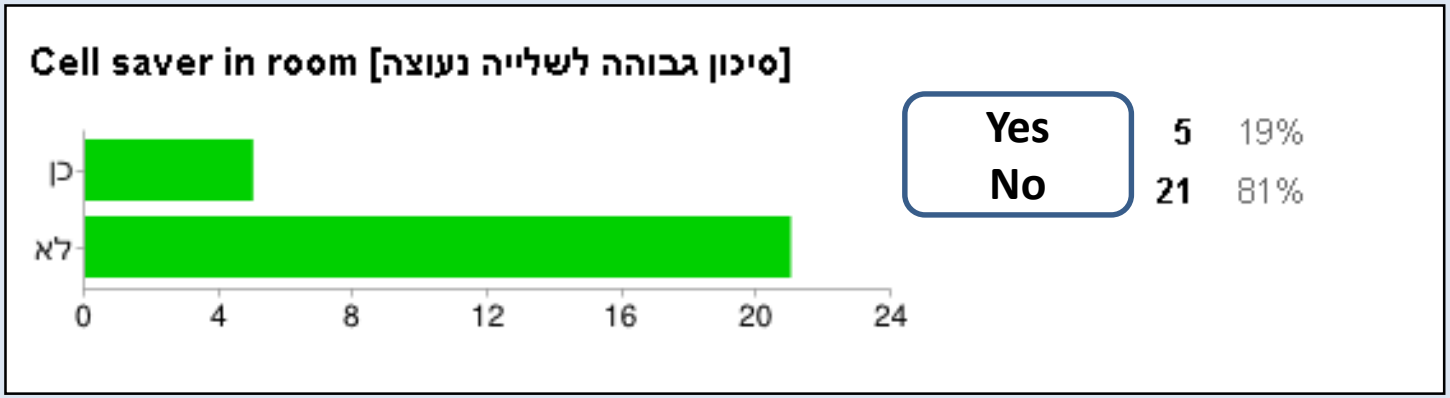
Cell saver technology in Israel for OB patient with high suspected peripartum bleeding

Archives of Gynecology and Obstetrics
February 2012, Volume 285, Issue 2, pp 281–284 | Cite as

Peripartum use of cell salvage: a university practice audit and literature review

Authors Authors and affiliations

Aharon Tevet, Sorina Grisaru-Granovsky, Arnon Samueloff, Alexander Ioscovich



ORIGINAL ARTICLE

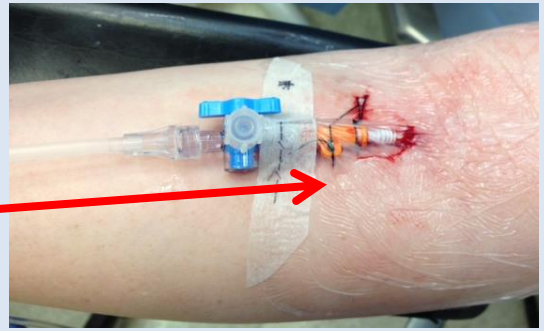
Israeli survey of anesthesia practice related to placenta previa and accreta

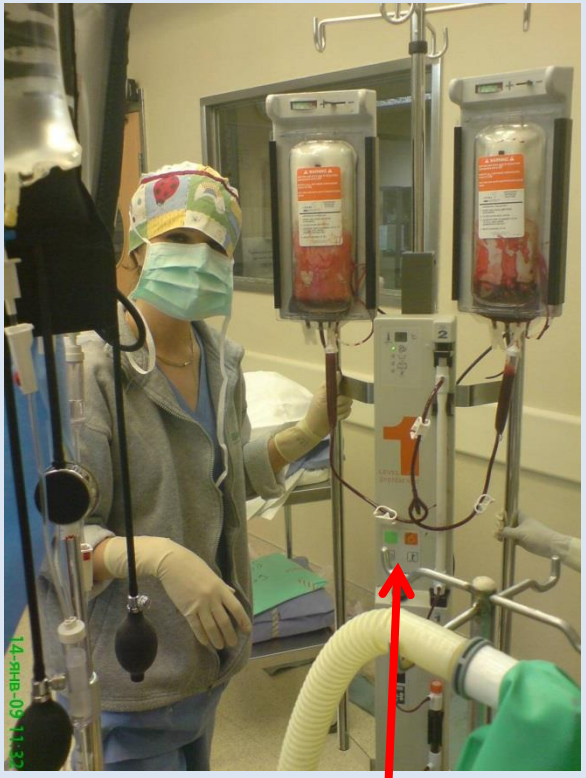
A. Ioscovich[1,*], D. Shatalin[1,*], A. J. Butwick[2], Y. Ginosar[3], S. Orbach-Zinger[4] and C. F. Weiniger[3]

[1]Department of Anesthesiology, Perioperative Medicine and Pain Treatment, Shaare Zedek Medical Center, Hebrew University, Jerusalem, Israel
[2] Department of Anesthesia, Stanford University School of Medicine, Stanford, California, USA
[3] Department of Anesthesiology and Critical Care Medicine, Hadassah-Hebrew University Medical Center, Ein Kerem, Jerusalem, Israel
[4] Department of Anesthesia, Rabin Medical Center (Beilinson Campus), Petah Tikvah, Tel Aviv University, Tel Aviv, Israel

Equipment

Two large-bore IV lines - 14-18G IV lines
High Flow 7.5 or 8 G





Arterial Line (Radial) for IBP monitoring and blood tests
Central Line - ???

TEE/FTTE
Trans Esophageal or Trans Thoracic Focused Echocardiography

Rapid infusion system
"Level one" system 0.5L/min warm solution

Protocols for massive bleeding

Blood products transfusion RATIO in massive trauma

PC : FFP - 1 : 1-1.4

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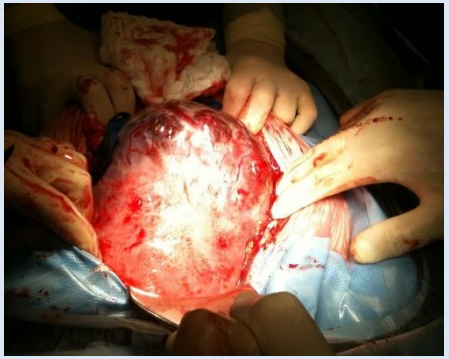


- Some obstetric centers have adopted formulaic protocols for PPH on data derived from massive trauma.
- Or **1:1:1:1 PC:FFP:PLT:CRYO**

Saule I, Hawkins N. Transfusion practice in major obstetric haemorrhage: lessons from trauma. *International Journal of Obstetric Anesthesia* 2012; **21**: 79–83.

The DISADVANTAGE of unmonitored "shock packs" transfusion

- FFP is donated from non-pregnant population
  - Fibrinogen < 2g/L
  - Relative low Factor VIII and von Willebrand
- Do not distinguish between the underlying **etiology of bleeding**
  - Early empirical FFP transfusion useful for placental abruption and amniotic fluid embolism (consumption mechanism) and unnecessary for atonic bleeding or genital tract trauma

Massive Hemorrhage protocols

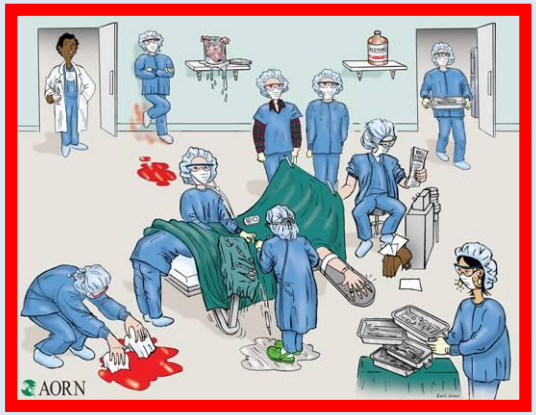
Using **massive obstetric hemorrhage protocols** is useful for facilitating rapid transfusion if needed, and can also be cost-effective.

Guasch E Med Intensiva. 2016 (Spain)
Massive obstetric hemorrhage: Current approach to management
A.J. Butwick Curr Opin Anaesthesiol 2015
Transfusion and coagulation management in major obstetric hemorrhage

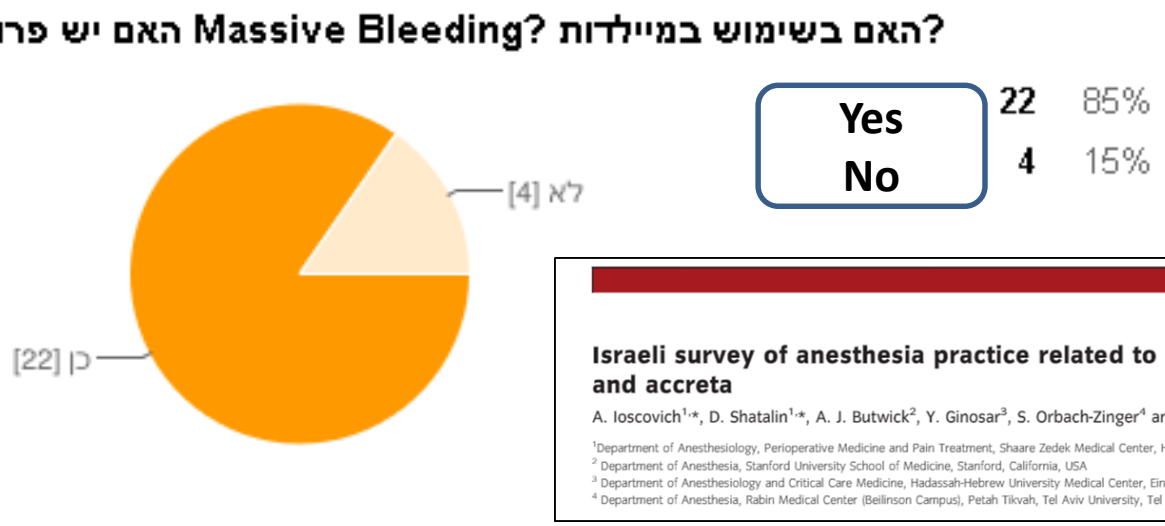
Original article | IJOA_2018_207

Retrospective Study to investigate fresh frozen plasma and packed cell ratios administered for women with postpartum hemorrhage before and after introduction of a massive transfusion protocol

Carolyn Weiniger, Alexander Gural, Alexander Ioscovich, Hen Sela, Noa Yakirevich-Amir, Sharon Einav



Transfusion protocols in Israel



ORIGINAL ARTICLE

Israeli survey of anesthesia practice related to placenta previa and accreta

A. Ioscovich[1,*], D. Shatalin[1,*], A. J. Butwick[2], Y. Ginosar[3], S. Orbach-Zinger[4] and C. F. Weiniger[3]

[1]Department of Anesthesiology, Perioperative Medicine and Pain Treatment, Shaare Zedek Medical Center, Hebrew University, Jerusalem, Israel
[2] Department of Anesthesia, Stanford University School of Medicine, Stanford, California, USA
[3] Department of Anesthesiology and Critical Care Medicine, Hadassah-Hebrew University Medical Center, Ein Kerem, Jerusalem, Israel
[4] Department of Anesthesia, Rabin Medical Center (Beilinson Campus), Petah Tikvah, Tel Aviv University, Tel Aviv, Israel

- **"Obstetric hemorrhage packs"**
- Availability of a local expert (hematologist or transfusion medicine physician) for consultation?
- **Laboratory assessment (every 15-30min)** ?

Table 1 Mechanisms of coagulopathy dependent on aetiology of obstetric bleed. Late onset is abnormal coagulation usually only after 2000 ml blood loss.

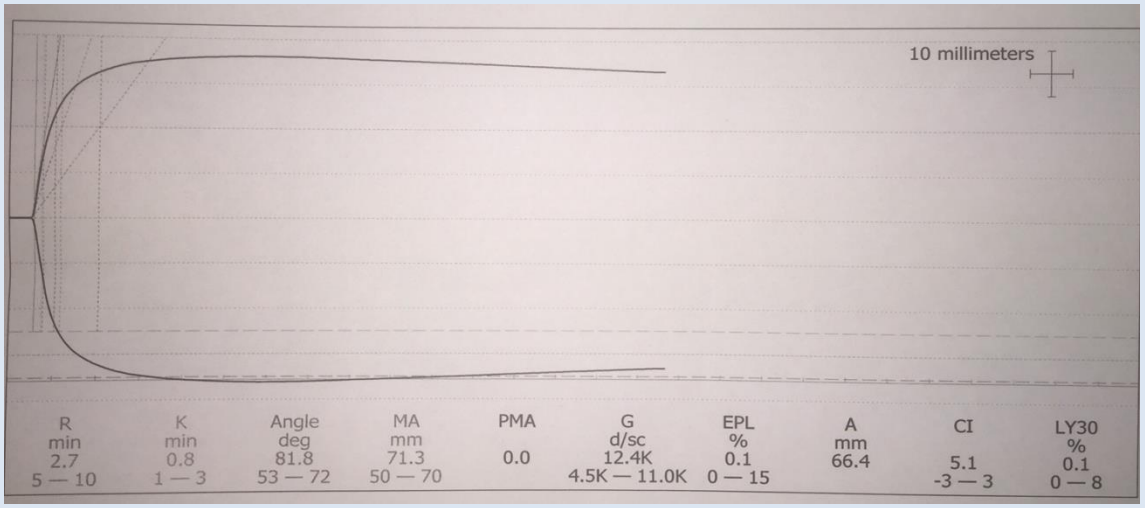
Aetiology of bleed	Likelihood of coagulopathy (% transfused FFP)	Time of onset of coagulopathy	Mechanism of coagulopathy		
			Dilution	Consumptive	
				Local to uterus and placenta	Disseminated intravascular
Uterine atony	14	Late	Contributes in severe cases	Contributes in severe case	Very rare
Genital tract or surgical trauma	4	Late	Contributes in severe cases	Contributes in severe cases	Very rare
Placental abruption	42	Early (often before blood loss observed)	Contributes in severe cases	Main cause in mild and moderate cases	Contributes in severe cases
Retained and adherent placenta	8	Early or late	Contributes in most cases	Contributes in some cases	Rare unless associated with infection
Uterine rupture	66	Early	Main cause because large bleeds are common	Contributes in some cases	–
AFE	100	Early	Contributes in large bleeds	–	Main cause
Pre-eclampsia/HELLP	ND	Early (often before labour)	Contributes in large bleeds	Contributes in some cases	Contributes in some cases

AFE, amniotic fluid embolus; HELLP, haemolysis, elevated liver enzymes and low platelets.

Mechanism of Coagulopathy

- Fibrinogen level after ~2L EBL due to uterine atonia or genital trauma was 3.9g/L with normal PT/aPTT
- In placental abruption ~2L EBL Fibrinogen level was 2.2g/L with normal PT/aPTT

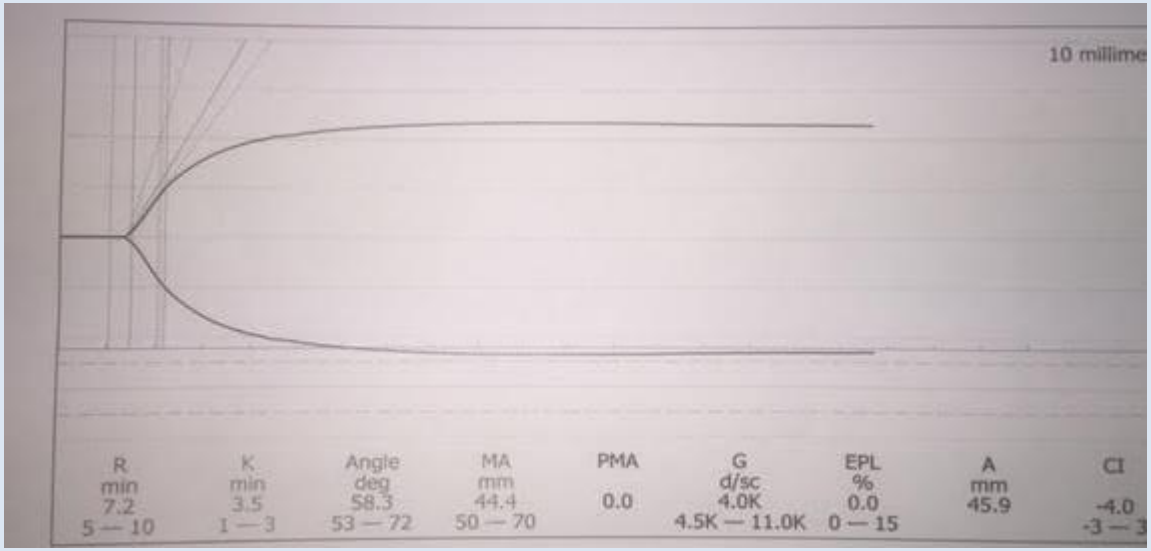
Collins PW, Lilley G, Bruynseels D, et al. Fibrin-based clot formation an early and rapidly biomarker for progression of postpartum hemorrhage: a prospective study. *Blood* 2014; **124**: 1727–36.



Atonic bleeding

EBL ~ 2.5-3 L

5 units PC



Total placental abruption

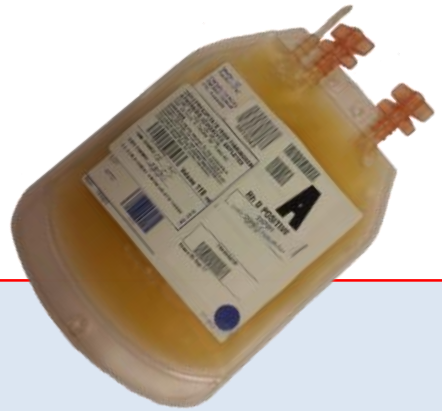
EBL ~ 3 L

6 units PC and 4 units FFP

6 units PLT

Cryoprecipitate for PPH

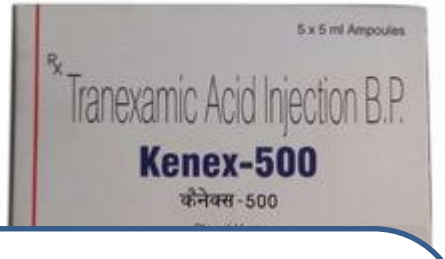
- Use of Cryoprecipitate to maintain the fibrinogen level above 1.5g/L if FFP has not be successful.
- 1 pool of Cryoprecipitate (~5 units) increase the fibrinogen level by 0.5g/L
- High concentration of Factor VIII and von Willebrand



Platelets in PPH

- Guidelines recommend PLT count > 50.000
- PLT should be infused when the count falls below 75.000 during ongoing PPH
- With exception of AFE, Severe preeclampsia and ITP low PLT is uncommon during PPH
- The strategy 1:1:1 PC:FFP:PLT would result in multiple PLT transfusion well above recommended levels.

Tranexamic acid



- ***Antifibrinolytic agents strengthen fibrin clots by inhibiting enzymatic fibrinolysis.***
- ***Blocks the degradation of fibrin clots by plasmin.***
- ***Have moderate but significant effect on blood loss.***
- ***Without significant adverse effects.***

The addition of tranexamic acid (1 g) is cheap, likely to be useful and appears safe.

Curr Opin Anaesthesiol. **2010 Jun;23(3):310-6**.
Use of clotting factors and other prohemostatic drugs for obstetric hemorrhage.
Mercier FJ , Bonnet MP.
Département d'Anesthésie Réanimation, Hôpital Antoine Béclère, Groupe Hospitalier Universitaire Paris Sud, Assistance Publique-Hôpitaux de Paris, Université Paris XI, Clamart, France. frederic.mercier@abc.aphp.fr

The current place of tranexamic acid in the management of bleeding.
Review article
Hunt BJ. Anaesthesia. 2015.

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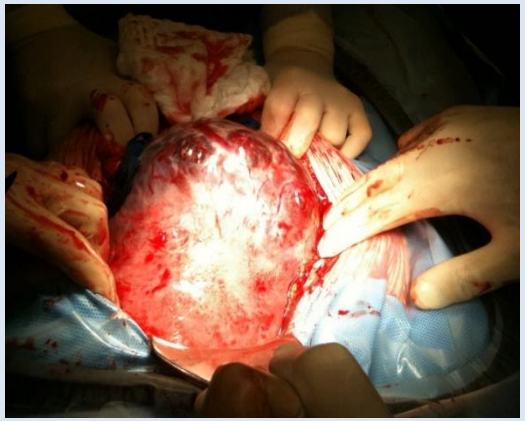


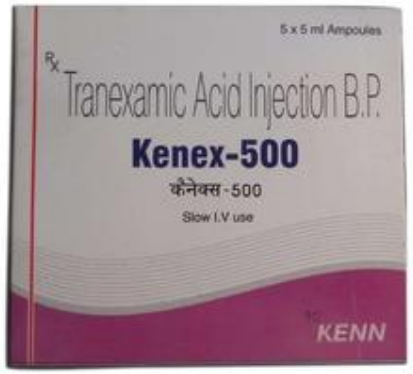
The CRASH 2 trial for trauma patients

Early administration of TXA safely reduced the risk of death in bleeding trauma patients.

The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients

Health Technology Assessment, 2013 Mar *No. 17.10*

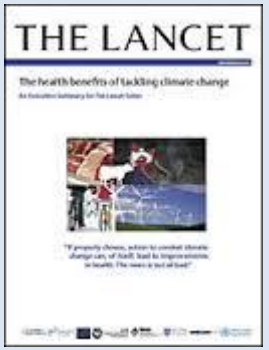
I Roberts, H Shakur, T Coats, B Hunt, E Balogun, L Barnetson, L Cook, T Kawahara, P Perel, D Prieto-Merino, M Ramos, J



The **WOMAN Trial** (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial. 15,000 women

Shakur H, et al. Trials. 2010.

World Health Organization and the European Society of Anesthesiology guidelines recommend 1gm Tranexamic Acid for > 1L Bleeding or for suspected massive bleeding



Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

*WOMAN Trial Collaborators**

www.thelancet.com **Published online April 26, 2017**

Death due to bleeding was significantly reduced in women given tranexamic acid (155 [1·5%] of 10 036 patients *vs* 191 [1·9%] of 9985 in the placebo group, risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045), especially in women given treatment within 3 h of giving birth (89 [1·2%] in the tranexamic acid group *vs* 127 [1·7%] in the placebo group,

A 10-year Update: National Survey Questionnaire of Obstetric Anesthesia Units in Israel

D. Shatalin, [a], C. F. Weiniger, [b,c]* I. Buchman, [a] Y. Ginosar, [b] S. Orbach-Zinger, [d] A. Ioscovich[a]*

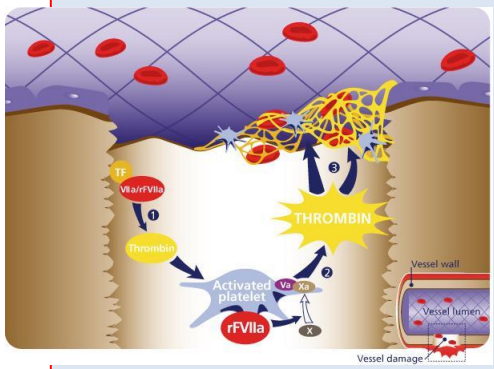
2017 (under revision in IJOA)

- In Israel in 2016 - 18 (72%) units tranexamic acid was routinely administered to women when postpartum hemorrhage occurred.

Recombination factor VII for peripartum bleeding (rFVIIa) (Novoseven)

FVIIa works via activation of the extrinsic pathway of the coagulation cascade leading to an enhanced generation of thrombin and a **stable fibrin plug at the site of injury.**

It was originally developed for the treatment of bleeding in patients with haemophilia



"Side-effects"

- Increased risk of thromboembolism **???**
- Costs of rFVII vs other treatment **$$$$$$**

Is it a hypercoagulated state of pregnant patients is a risk factor for embolic event ?

Recombinant activated factor VII (rFVIIa, NovoSeven) was used in three patients with massive obstetric hemorrhage due to

- **placenta previa accreta**
- **rupture of the uterus and**
- **pre-eclampsia with HELLP**

Administration of the drug markedly decreased the bleeding and enabled control of the hemorrhage. **rFVIIa seems to be an adjunctive haemostatic measure for the treatment of severe obstetric hemorrhage.**

Arch Gynecol Obstet. 2003 Oct;268(4):266-7.

Treatment of obstetric hemorrhage with recombinant activated factor VII (rFVIIa).

Segal S Department of Obstetrics and Gynecology, Ben-Gurion University of The Negev, Barzilai Medical Center, Ashkelon, Israel 78306.

Thus, the timely use of rFVIIa, hence, can be used to save life and fertility in cases of intractable obstetric bleeding.

Indian J Anaesth. 2012 Jan;56(1):69-71.
Burad J, Bhakta P, Sharma J.
Department of Anaesthesia and Intensive Care, Sultan Qaboos University Hospital, Muscat, Oman.

Pulmonary embolism after administration of recombinant activated Factor VII for major obstetric hemorrhage.
J Clin Anesth. 2012 Sep;24(6):508-9. McCarthy GC, Allen TK, Habib AS.

For intraoperative NONSURGICAL bleeding

1- Normal Fibrinogen level
2- pH close to 7.35-7.4
3- Normothermia

World Health Organization. WHO Guidelines for the Management of Postpartum Haemorrhage and Retained Placenta. http://apps.who.int/iris/bitstream/10665/75411/1/9789241548502_eng.pdf (accessed 17/09/2014).

Fibrinogen concentrates in postpartum hemorrhage

- Human plasma-derived fibrinogen concentrates are **now available in most countries but not everywhere.**
- **10 randomized controlled trials have explored the potential benefit** of fibrinogen concentrates in terms of transfusion requirement and correction of hemostasis disorders.
- The "FIB-PPH Trial", as it is known, is a Danish multicenter placebo-controlled, double-blinded clinical trial evaluating whether initial treatment with **fibrinogen concentrate (2 g) reduces the need for allogenic blood transfusion in PPH.**
- **"Therefore, we still need valid data before administration of fibrinogen concentrate as a curative treatment of PPH can be firmly recommended."**

F1000Research F1000Research 2016, 5(F1000 Faculty Rev):1514 Last updated: 27 JUN 2016

REVIEW

Management of postpartum haemorrhage [version 1; referees: 2 approved]

Marie Pierre Bonnet[1], Dan Benhamou[2]

[1]Department of Anaesthesia and Intensive Care Medicine, Paris Descartes University, Paris, France
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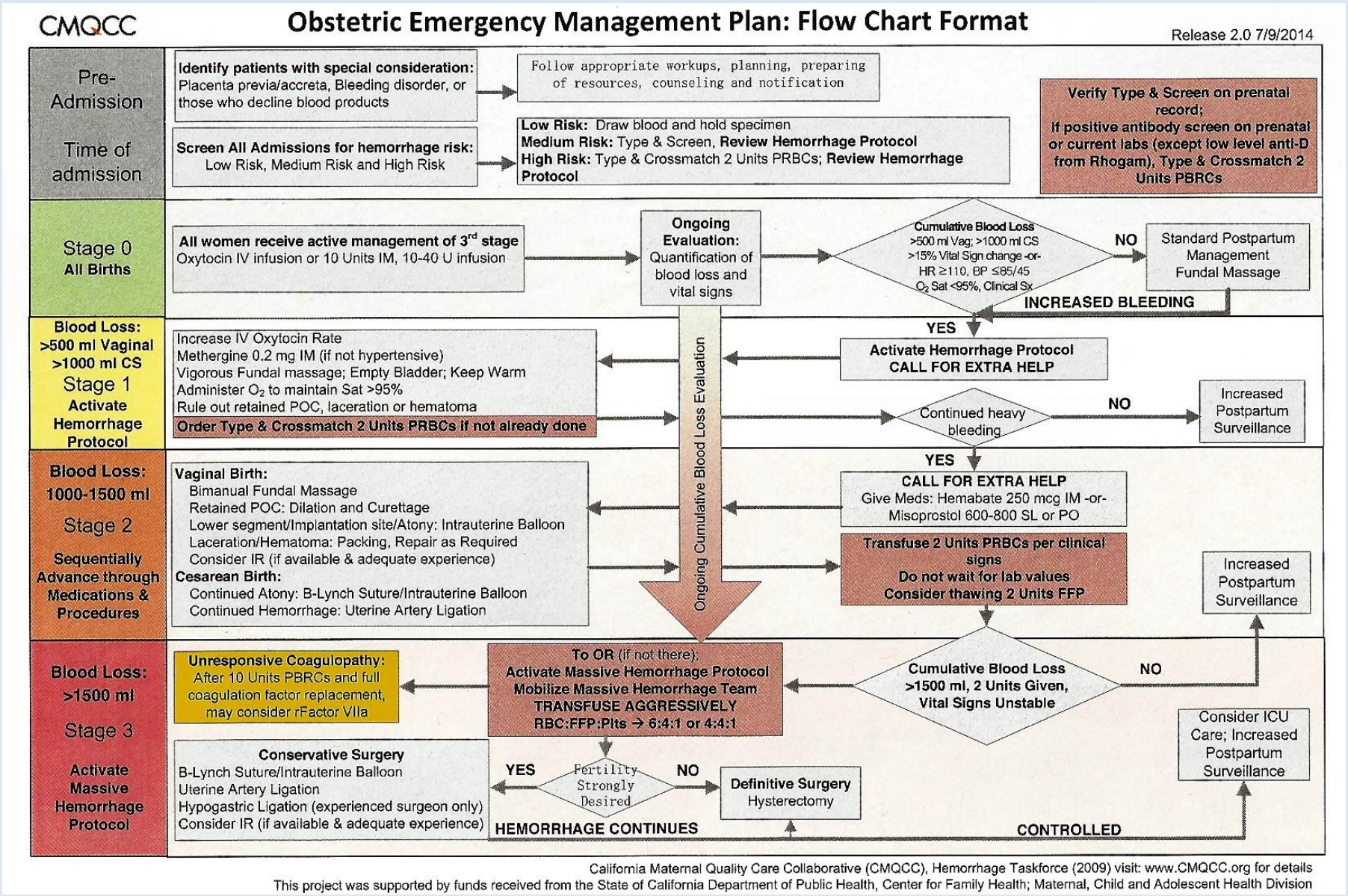
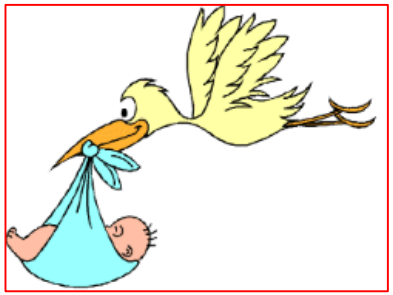


California Maternal Quality Care Collaborative Hemorrhage Taskforce, www.CMQCC.org, March 2015

Summary

- Rate of Post Partum Hemorrhage (PPH) grow up
- Massive PPH ≠ Massive trauma-associated hemorrhage
- EBL is usually underestimated
- Monitoring (Fibrinogen; TEG or ROTEM; SpHb®)
- Equipment (Cell saver, Level 1, Echocardiography)
- Institutional protocol for PPH
- Blood Products
- Tranexamic acid ± Fibrinogen concentrates
- Recombinant activated factor VII (rFVIIa)?
- Team Approach !!!
- *Uterotonic drugs and devices*
- *Invasive radiology*



Съезд Congress

5-7 сентября 2018 / Санкт-Петербург
September 5-7, 2018 / St. Petersburg

Thank you!!!