

Patient Blood Management in Obstetrics

Christine Lett MD FRCSC
Transfusion Symposium
October 26, 2018



Objectives

- Describe the risks of anemia and iron deficiency in obstetrics
- Discuss transfusion in OB
- Review the role of tranexamic acid in OB
- Present the local OB PBM Research Report
- Describe future directions for PBM in OB

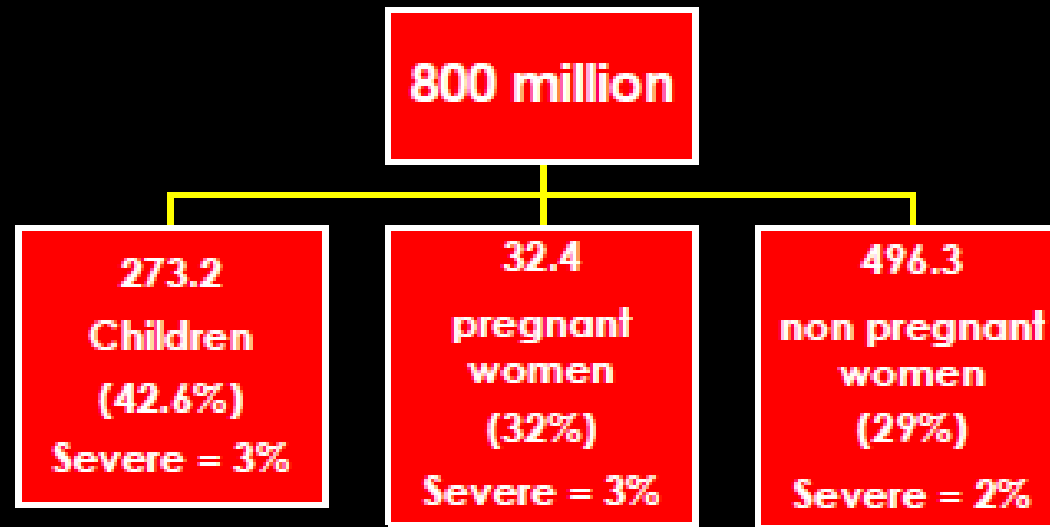
Introduction

- Iron deficiency is the most common micronutrient deficiency in the world
 - 100x more prevalent than cancer
- Anemia in pregnancy definition (WHO)
 - **Hb <110 g/L or hct <33%**
 - Severe anemia Hb <70 g/L
- Physiologic anemia of pregnancy resolves by 6 weeks postpartum

Global Anemia In Women And Children

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How Big Is The Problem?



Global prevalence of anemia in 2011. WHO

OB RISKS OF ANEMIA

Mom

- Fatigue
- Poor exercise tolerance
- Poor work performance
- Preeclampsia
- Transfusion
- Cardiac failure / death

Baby

- Miscarriage
- SGA / LBW
- Preterm delivery
- IUFD
- Abruptio
- C-section
- Apgar <7 at 5 minutes
- Poor cognitive and motor development
- Long term memory impairment

Journal of Nutrition

Journal of American Clinical Nutrition

Mother-Infant Interactions and Infant Development Are Altered by Maternal Iron Deficiency Anemia¹

Eva M. Perez, Michael K. Hendricks, John L. Beard,^{*2} Laura E. Murray-Kolb,^{*} Astrid Berg, Mark Tomlinson, James Irlam, Washiefa Isaacs, T. Njengele, Alan Sive, and Lynne Vernon-Feagans[†]

Maternal Iron Deficiency Anemia Affects Postpartum Emotions and Cognition¹

John L. Beard,² Michael K. Hendricks,^{*} Eva M. Perez,^{*} Laura E. Murray-Kolb, Astrid Berg,^{*}

Is There a Causal Relationship between Iron Deficiency or Iron-Deficiency Anemia and Weight at Birth, Length of Gestation and Perinatal Mortality?^{1,2}

Kathleen M. Rasmussen

Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853.

Low Hemoglobin Level Is a Risk Factor for Postpartum Depression¹

(Manuscript received 21 August 2003. Initial review completed 15 September 2003. Revision accepted 26 September 2003.)

Elizabeth J. Corwin,² Laura E. Murray-Kolb^{*}
and John L. Beard^{*}



Published in final edited form as:

J Pediatr. 2012 June ; 160(6): 1027–1033. doi:10.1016/j.jpeds.2011.12.011.

Iron deficiency in infancy is associated with altered neural correlates of recognition memory at 10 years

Eliza L. Congdon, BS¹, Alissa Westerlund, BA¹, Cecilia R. Algarin, MD², Patricio D. Peirano, MD, PhD², Matthew Gregas, PhD¹, Betsy Lozoff, MD⁴, and Charles A. Nelson, PhD^{1,3}

Mechanisms:

1. Reduced myelination by oligodendrocytes in utero and first few weeks of life. Irreversible.
2. Dopamine and Norepinephrine signaling in the brain is altered. Partially reversible.
3. Cytochrome oxidase activity is reduced in iron deficient infants; ATP production, particularly in the hippocampus, is reduced.

Economic Burden of Anemia

Global Anemia In Women And Children

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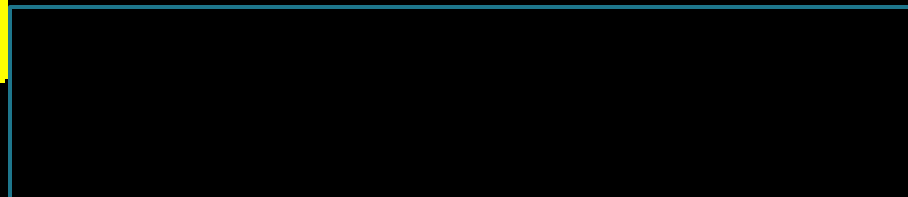
ECONOMIC IMPACT ANEMIA

Anemia

↓ Productivity

Loss of
income

Loss of
human
workforce



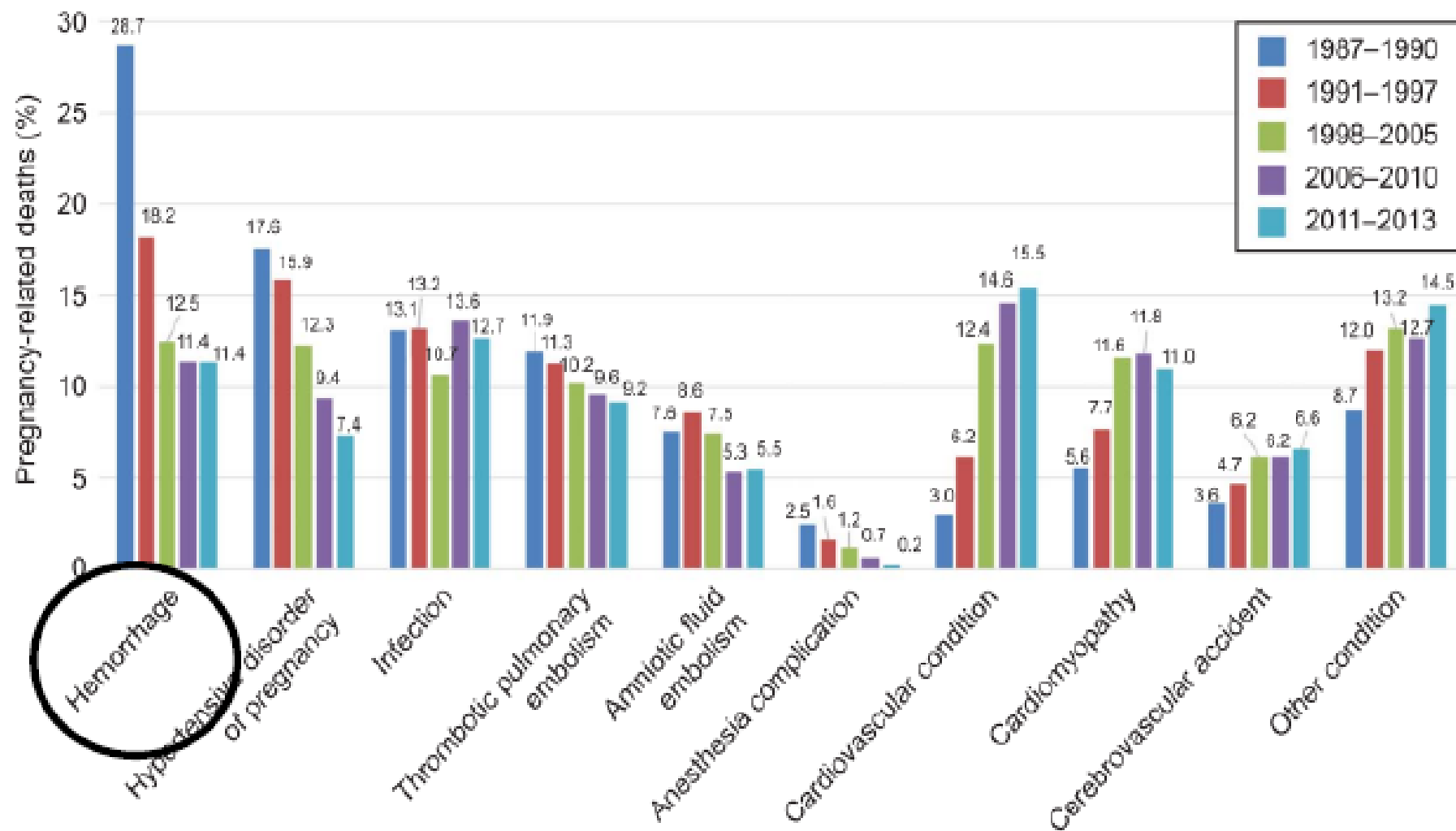
Economic Burden of Anemia

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ECONOMIC IMPACT ANEMIA





Creanga. *Obstet Gynecol* 2017; 130: 366-73

Hemorrhage is a leading cause of maternal death



Patient Blood Management is the timely multidisciplinary application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in effort to improve patient outcome

○ Transfusion

- 1. Don't transfuse blood if non-transfusion therapies or observation would be as effective
- 2. Don't give more than one unit at a time in a stable patient

○ Hematology

- 5. Don't transfuse patients based solely on an arbitrary hemoglobin threshold.

○ Internal Medicine

- 3. Don't transfuse red blood cells for arbitrary hemoglobin or hematocrit thresholds in the absence of symptoms, active coronary disease, heart failure or stroke.
- 5. In the inpatient setting, don't order repeated CBC and chemistry testing in the face of clinical and lab stability.

Transfusion in OB

Transfusion “threshold”

Risks specific to the OB population

Fibrinogen concentrate

Hb < 5g/dL

<u>Year</u>	<u>Recommendation</u>	<u>Society</u>	Hb < 5g/dL
1988	<7g/dl	NIH	

Table I - Haemoglobin (Hb) thresholds for packed red cell transfusion, according to the patients' characteristics.

Patient's characteristics	Transfusion threshold*
Sub-acute anaemia in asymptomatic young patients	Hb <5 g/dL
Sub-acute anaemia in young patients with signs/symptoms** and without risk criteria ***	Hb <6 g/dL
Sub-acute anaemia in older patients with signs/symptoms and without risk criteria	Hb <7 g/dL
Sub-acute anaemia in patients with risk criteria and without signs/symptoms	Hb <8 g/dL
Sub-acute anaemia in patients with risk criteria and signs/symptoms	Hb <9 g/dL

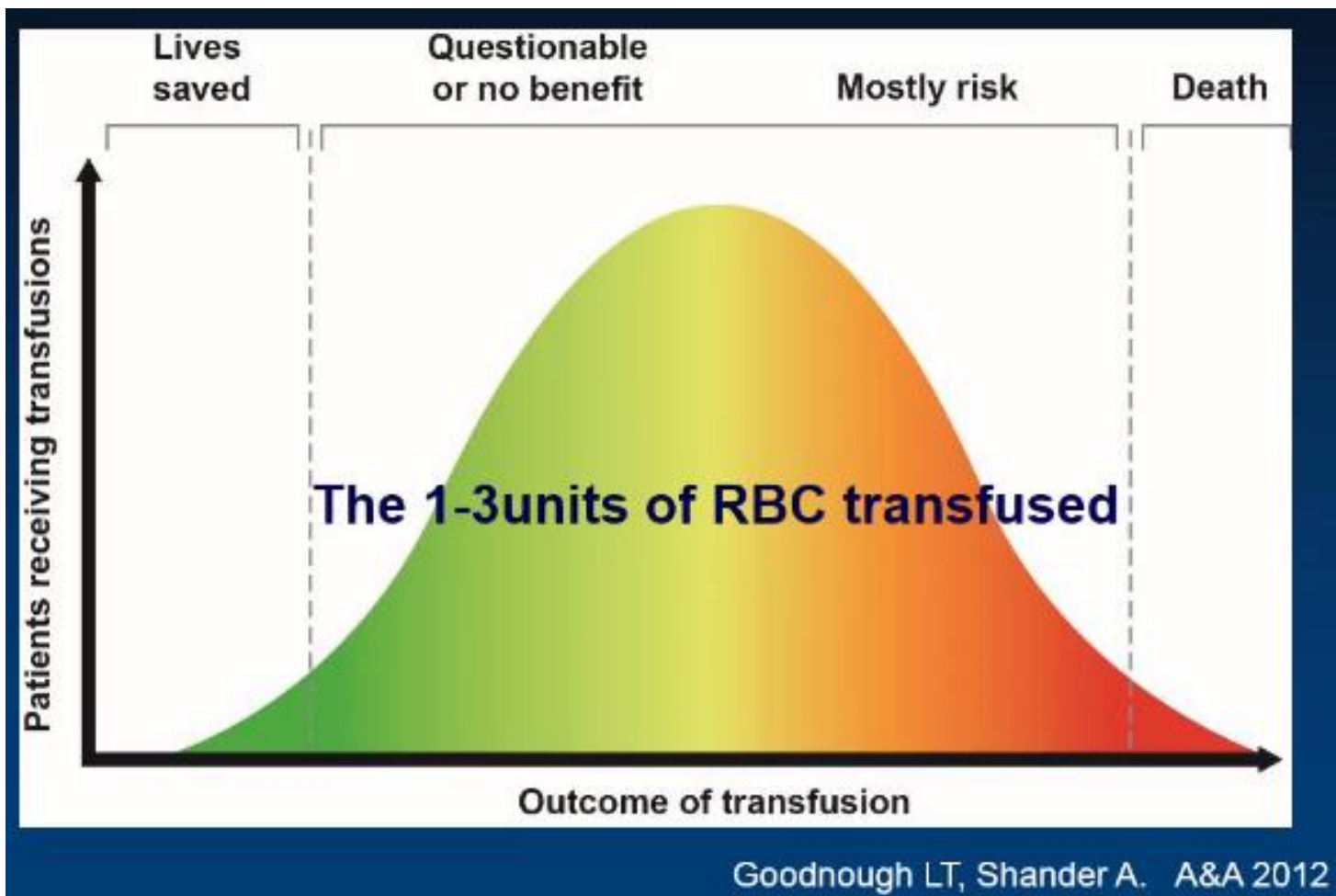
*Adapted from the Recommendations from the Spanish Society for Blood Transfusion and Cellular Therapy¹³; **Clinical signs/symptoms: hypotension, tachycardia, tachypnoea, dizziness or fatigue; ***Risk criteria: coronary or valvular disease, heart failure, vascular cerebral disease chronic pulmonary obstructive disease, etc.

<u>Year</u>	<u>Recommendation</u>	<u>Society</u>
2016	7g/dl	AABB/AMA

RBC transfusions result in

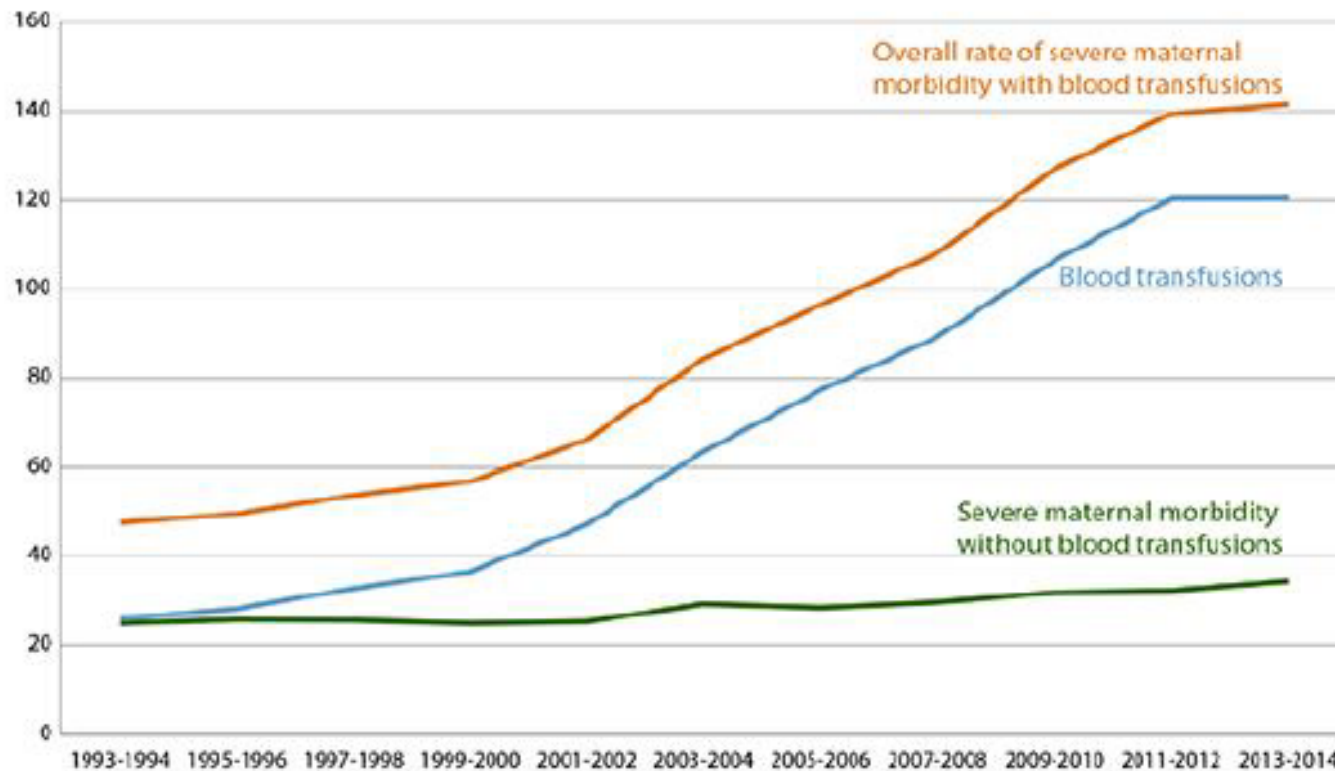
- ◆ **Mortality ↑**
- ◆ **Length of hospital stay ↑**
- ◆ **Organ dysfunction ↑**
 - Lung injury (TRALI, TACO)
 - Renal impairment
 - Stroke
 - Myocardial infarction
- ◆ **Infection ↑**
- ◆ **Transfusion reactions**
- ◆ **Tumor growth promotion ↑**
- ◆ **Costs ↑**
- ◆ **Non-Hodgkin lymphoma ↑**

Spahn D. R. et al. Lancet (2013) 381: 1855





Rates of Severe Maternal Morbidity per 10,000 Delivery Hospitalizations



PPH – WOMB Trial

- ▶ 37 Dutch hospitals, 521 women randomized
- ▶ PPH with >1000 ml, Hb drop of 19+ points, and hemoglobin between 48-79 g/L, no severe symptoms of anemia (dyspnea, syncope, HR>100)
- ▶ Randomized to transfusion or no transfusion

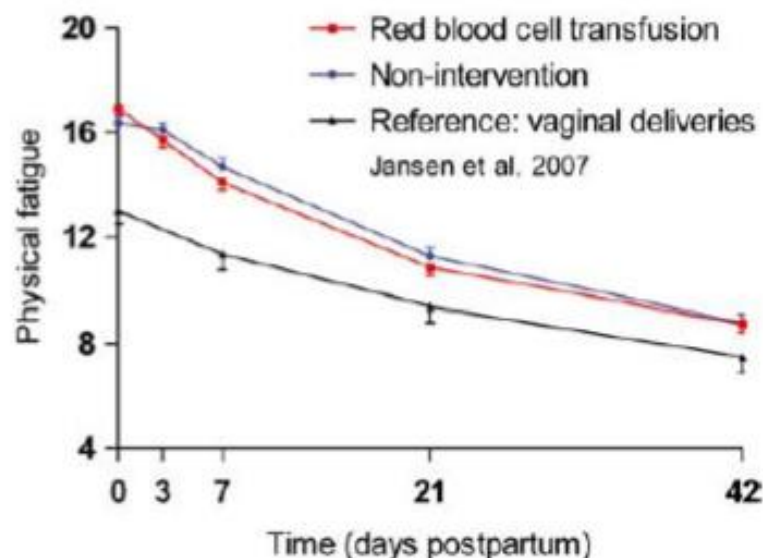


Table 2. Blood loss, haemoglobin concentration, and RBC transfusion

Variable	Transfusion (n = 258)	Non-intervention (n = 261)	P
RBC transfusion			
Units per woman	2 (2-2)	0 (0-0)	<0.001
Total units*	517	88	<0.001
Hb concentration after transfusion, g/dl)**	9.0 (8.5-9.6)	8.9 (8.2-9.7)	0.56
Hb concentration at discharge (g/dl)***	9.0 (8.5-9.5)	7.4 (6.8-7.7)	<0.001
Hb concentration at 6 weeks (g/dl)****	12.1 (11.3-12.6)	11.9 (10.9-12.6)	0.18

Single-dose intravenous iron infusion versus red blood cell transfusion for the treatment of severe postpartum anaemia: a randomized controlled pilot study

C. Holm,^{1,2} L. L. Thomsen,² A. Norgaard³ & J. Langhoff-Roos¹

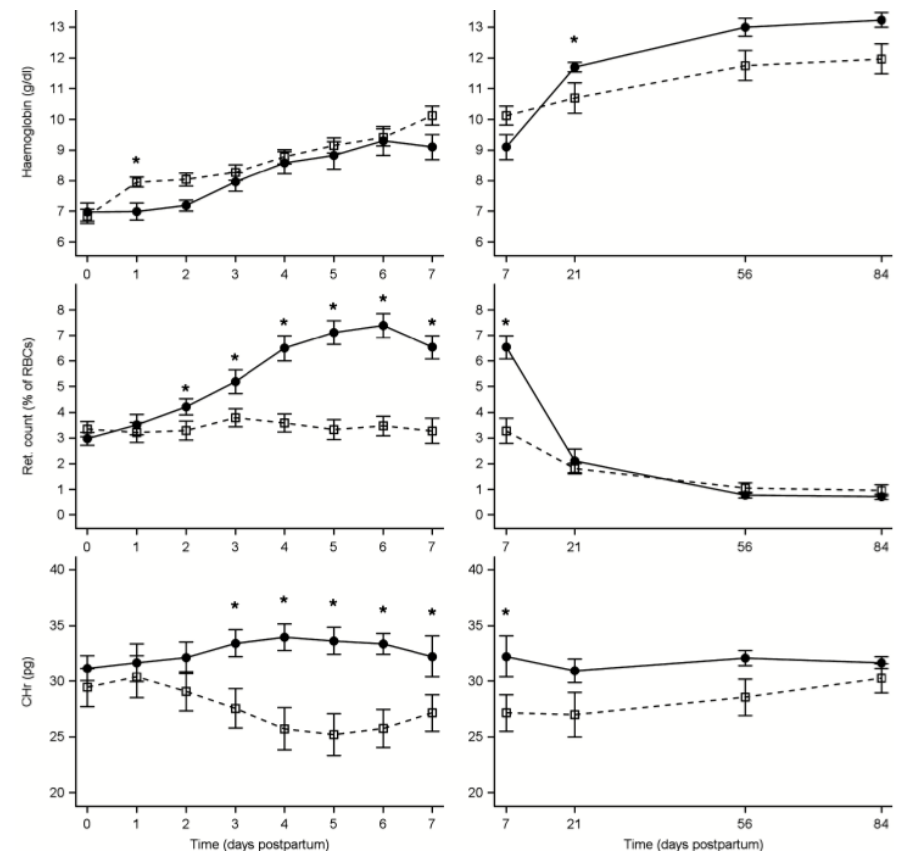
¹Department of Obstetrics, Juliane Marie Centre, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

²Pharmacosmas A/S, Holbaek, Denmark

³Section for Transfusion Medicine, Capital Region Blood Bank, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

Hb higher in transfusion group first week

Hb, Hb density of reticulocytes, ferritin, TIBC, %sat all higher in iron group after 3 weeks



Antepartum Anemia RCT PO vs. IV iron

- Early outcomes in favor of IV iron:
 - higher Hb, higher ferritin
- 3 years later – f/u data in favor of IV iron:
 - Improved health related quality of life scores during pregnancy for 3 years
 - Higher ferritin and Hb long-term
 - Less postpartum depression
 - Longer breastfeeding

Guidelines

RCOG PPH guideline 2016:

Antenatal anemia should be investigated and treated appropriately as this may reduce morbidity with PPH

NATA consensus statement 2017

British Committee for Standards in Haematology 2011

- Screening (CBC) at booking at 28 weeks
- Oral iron is first line for anemia and iron deficiency without anemia (ferritin <30)
- IV iron should be used if
 - Hb <80g/L
 - >34 weeks
 - Inadequate response to IV iron
 - Postpartum and Hb <90 g/L
- Consider transfusion if Hb <60g/L if
 - Symptoms of ischemia
 - High risk of further bleeding

Long-term risks of transfusion in OB



NIH Public Access

Author Manuscript

Transfus Med Rev. Author manuscript; available in PMC 2014 January 01.

Published in final edited form as:

Transfus Med Rev. 2013 January ; 27(1): 10–20. doi:10.1016/j.tmr.2012.08.002.

Transfusion Associated Microchimerism: The Hybrid Within

Evan M Bloch, MD, MS¹, Rachael P Jackman, PhD, Tzong-Hae Lee, MD, PhD¹, and Michael P Busch, MD, PhD¹

- Chimera
- ?Increased autoimmune disease

Long-term risks of transfusion in OB

- Alloimmunization
 - Risk of alloimmunization
 - 1:13 with any blood transfusion
 - 1:18 if Rh negative and we forget WinRho

Fibrinogen concentrate

FFP vs. fibrinogen concentrate:

- Pregnancy is a hypercoagulable state
- FFP does not come from pregnant donors
- FFP may dilute physiologic pregnancy levels of coagulation factors

	Fibrinogen g/L
Non-pregnant	2.3 – 5.0
First trimester	2.4 – 5.1
Second trimester	2.9 – 5.4
Third trimester	3.7 – 6.2

Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. Obstet Gynecol. 2009 Dec;114(6):1326-31. PMID:[19935037](#)

Take home message => consider Fibrinogen concentrate early in OB – MHP
(Off label use!)

Tranexamic acid in OB



Lancet 2017; 389: 2105–16

WOMAN trial

RCT

- 20,060 women with PPH following delivery from 193 hospitals in 21 countries
- Intervention:
 - Tranexamic acid 1g IV +/- one repeat dose if ongoing bleeding within 24 hours

Outcomes:

- **Decreased death due to bleeding with TXA**
 - RR 0.81, 95% CI 0.65–1.00; p=0.045
 - RR 0.69, 95% CI 0.52–0.91; p=0.008
 - **Mortality benefit more pronounced if TXA given within 3 hours**

Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: a meta-analysis of individual patient-level data from 40 138 bleeding patients

Lancet 2018; 391: 125-32

Angèle Gayet-Ageron, David Prieto-Merino, Katharine Ker, Haleema Shakur, François-Xavier Ageron, Ian Roberts, for the Antifibrinolytic Trials Collaboration*

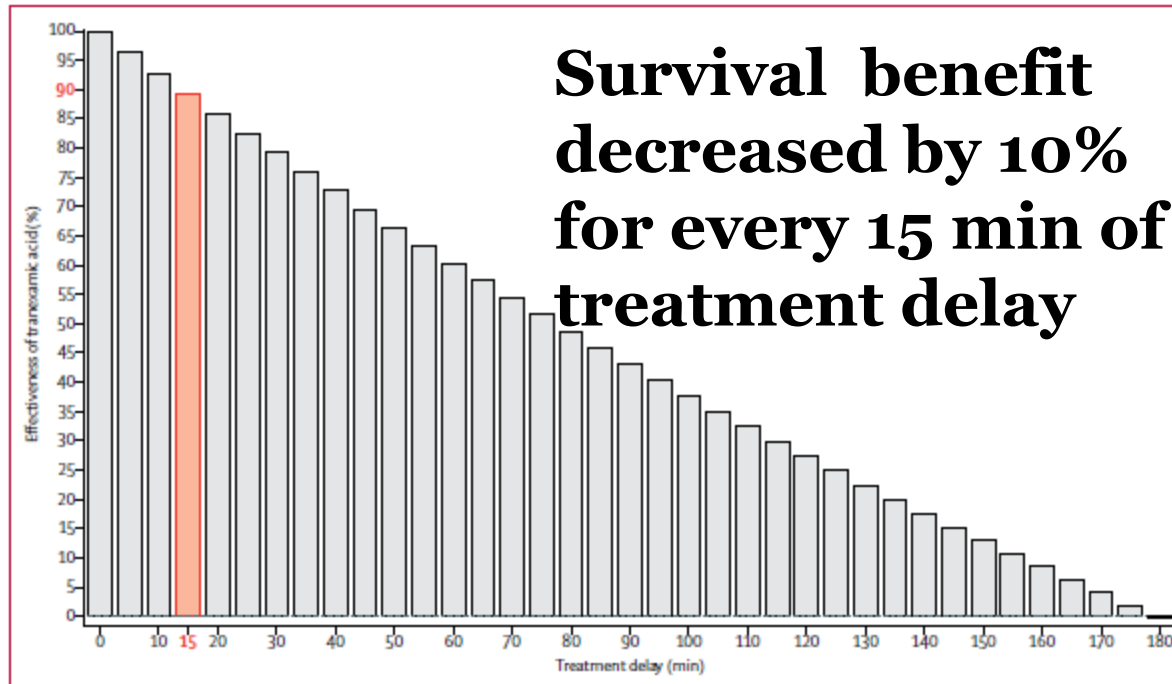


Figure 4: Reduction in effectiveness of tranexamic acid with increasing treatment delay

The bars represent the estimated treatment effectiveness (y-axis, estimated by $[(OR \text{ at time } t-1)/(OR \text{ at } t-0-1) \times 100]$ in %) at 5-min intervals of treatment delay. The bar highlighted in red shows the estimated treatment effectiveness (90%) with a treatment delay of 15 min.

- Immediate treatment improved survival by >70% (OR 1.72 95% CI 1.42-2.10; $p < 0.0001$)
- No increase in vascular occlusive events with TXA
- **No benefit if tranexamic acid given after 3 hours**

Tranexamic acid in PPH

European Society of Anesthesiology 2016:

“We recommend the administration of tranexamic acid in PPH at a dose of 1g IV as soon as possible, which can be repeated if bleeding continues” IB

Eur J Anaesthesiol 2017; **34**:332–395

Local Research Report

Type & Screens in OB

Appropriateness of blood transfusion in OB

Iron deficiency in pregnancy

Original Research

Hospital-acquired anemia: Prevalence, outcomes, and healthcare implications

Colleen G. Koch MD ✉, Liang Li PhD, Zhiyuan Sun MS,



75% of patients will
become anemic during
their hospital stay

90% of that anemia will be
iatrogenic

2013 British Journal Of Hematology
**Average Daily Blood
Draws = 40mL**

Physiologically (and under ideal circumstances)
the most blood a human can make in a day is

40mL

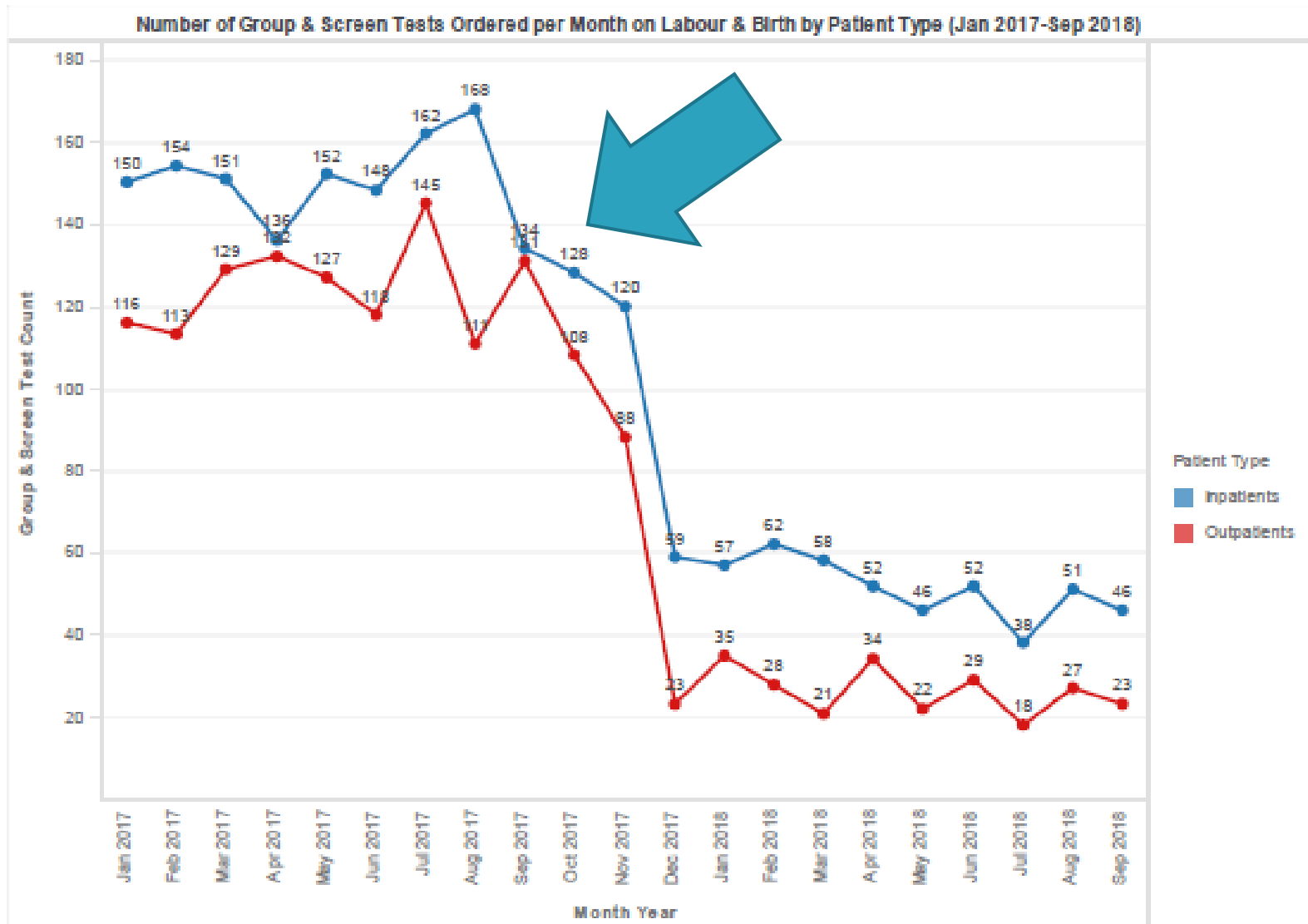
Type and screen in OB

- Stop unnecessary phlebotomy
- Reduce cost (\$166/type & screen)

Prior to elective c-section	on MBU	on L&D
Jan – June 2017 = 197	2017 = 225	2017 = 1573
Jan – June 2018 = 60	2018 = 390	2018 = 445

- Cost savings \$182,600 in 6 months

Type and Screen on Labor & Birth



Appropriateness of RBC transfusion in OB

Dr. Peter Thiel, Dr. Erwin Karreman, Dr. Christine Lett

- Review all OB transfusions Jan 1 – Dec 31, 2016
- Appropriate if:
 - **Stable (not actively bleeding) all 3 criteria required:**
 - initial hemoglobin <70 g/L
 - post-transfusion hemoglobin <90 g/L
 - a single unit of packed red cells is ordered, with reassessment of patient's clinical condition and hemoglobin prior to the ordering of subsequent units
 - **Actively bleeding: one of the following required**
 - post-transfusion hemoglobin <100 g/L
 - ≥ 5 units given

Appropriateness of RBC transfusion in OB

Dr. Peter Thiel, Dr. Erwin Karreman, Dr. Christine Lett

- Results

- 58 patients transfused (71 transfusion events)

1.4% of all OB patients admitted

- Transfusion appropriate

48%

Stay tuned ...
2018 data pending

- Characteristics of inappropriate transfusion events

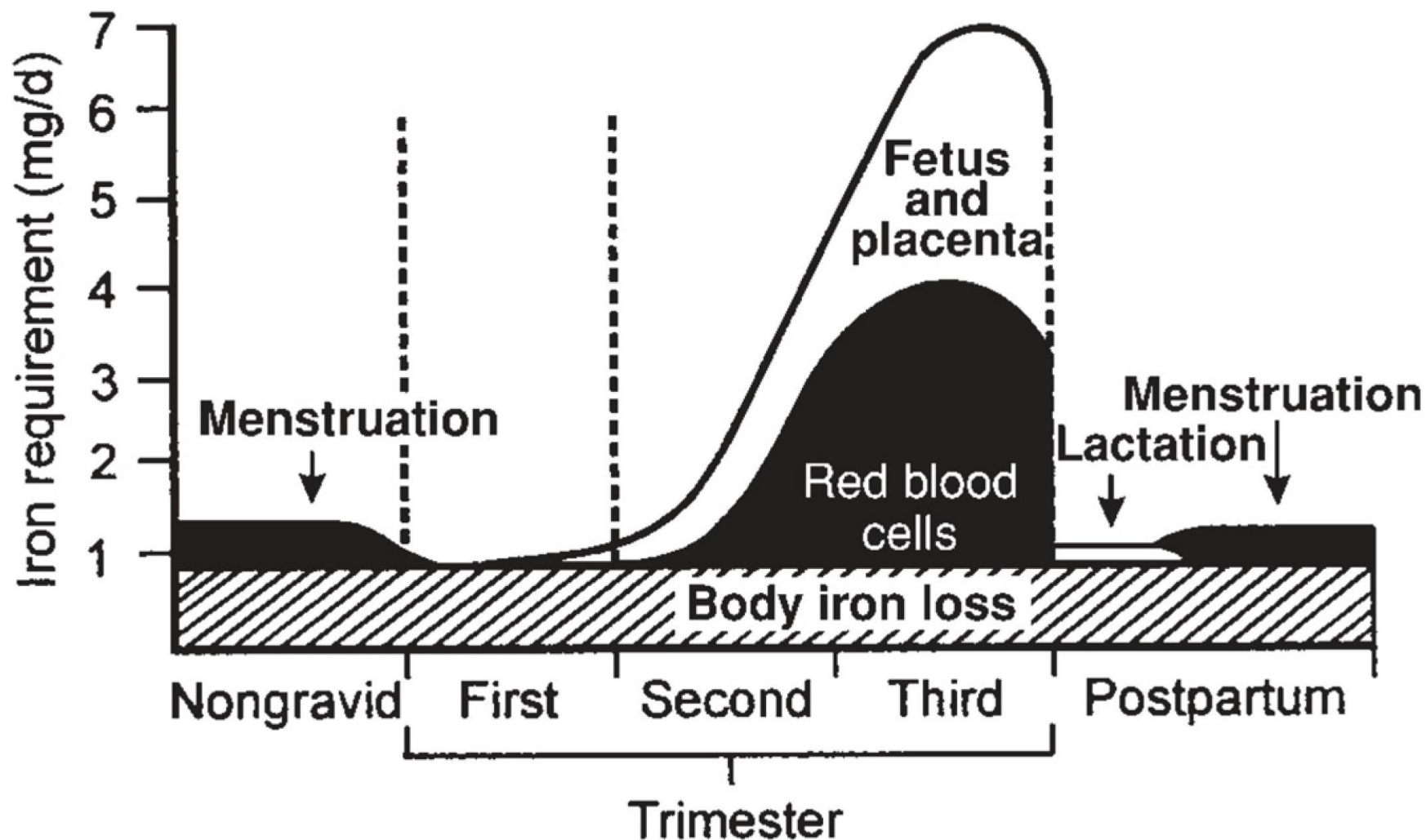
n=37

Not actively bleeding 30

No reassess after 1 unit 25

Over-transfused 13

Iron requirements in pregnancy



Iron deficiency in Pregnancy: a commonly unrecognized problem

Dr. Kirsti Ziola, Dr. Erwin Karreman, Dr. Christine Lett

Objectives:

- 1) Determine the incidence of iron deficiency and anemia during pregnancy and postpartum
- 2) Determine the impact of iron supplementation on pre-delivery and postpartum anemia in iron deficient patients.

Iron deficiency in Pregnancy: a commonly unrecognized problem

Dr. Kirsti Ziola, Dr. Erwin Karreman, Dr. Christine Lett

Methods:

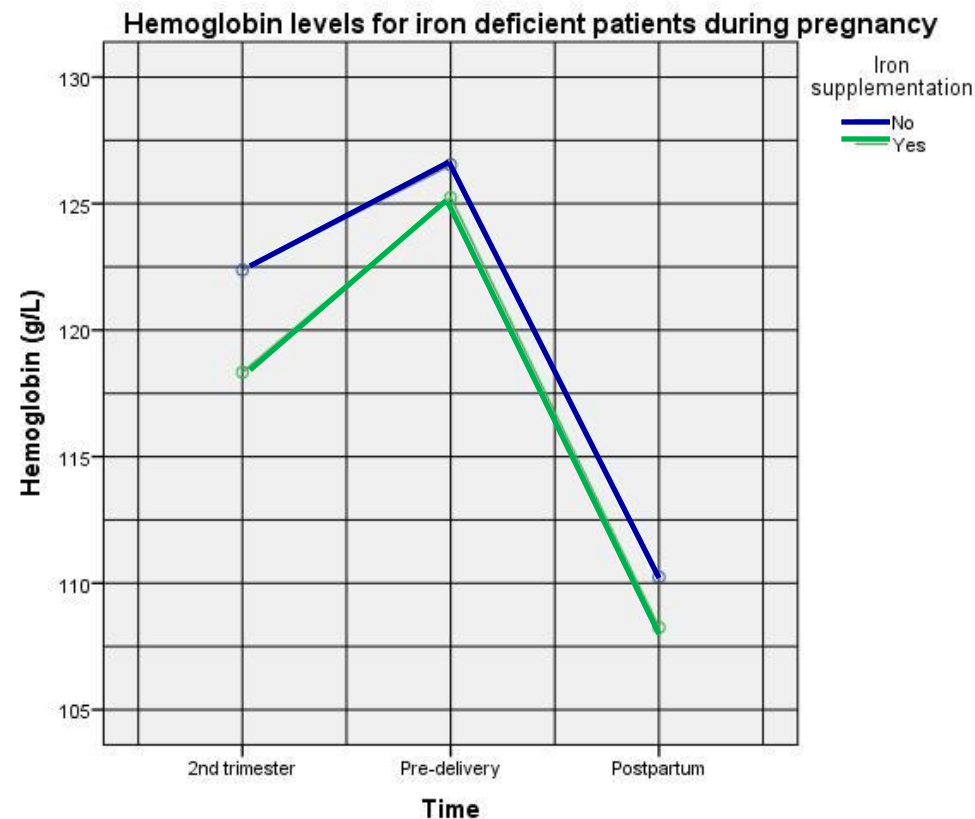
- Retrospective review of 280 patients between November 2016 and November 2017 was performed using an office EMR
- CBC, iron, %saturation, and ferritin were performed with second trimester diabetes screening
- Definitions:
 - **Anemia** = hemoglobin <110g/L
 - **iron deficiency** = ferritin < 30 ng/mL and/or %saturation < 15%
- Iron deficiency was treated with antepartum oral iron supplementation at the discretion of the care provider.
- Hemoglobin values pre-delivery and postpartum were recorded.

Iron deficiency in Pregnancy: a commonly unrecognized problem

Dr. Kirsti Ziola, Dr. Erwin Karreman, Dr. Christine Lett

Results:

- 24-28 weeks
 - **87% were iron deficient**
 - **8% were anemic**
- Postpartum
 - **44% were anemic**
- 74% of iron deficient women received PO iron



Future Directions: What I learned about at SABM

Quantitative Blood Loss

Massive Hemorrhage Protocol – OB hemorrhage bundle

TEG

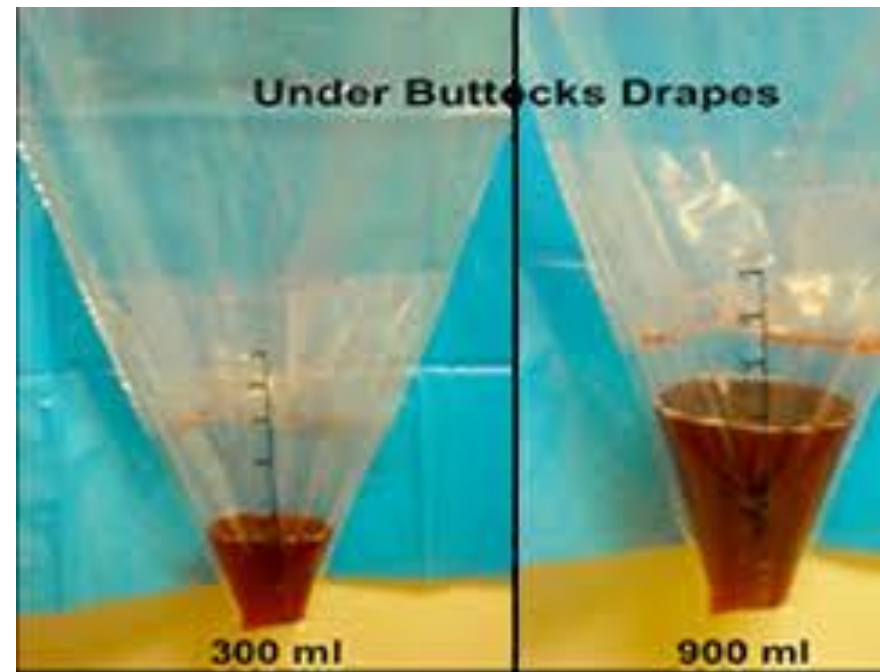
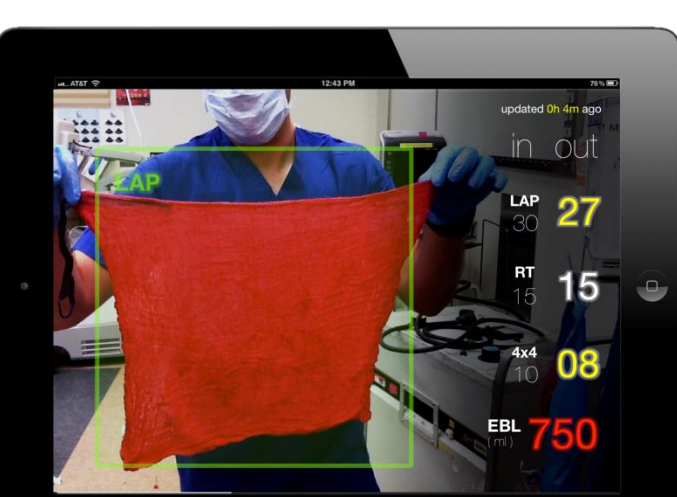


Quantitative Blood Loss (QBL)

- Why do we accept an estimate of blood loss?
 - Visual estimation of large blood loss underestimates by 35-50%¹

Quantitative Blood Loss methods

- Volumetric
- Gravimetric
- Triton L&D



¹CMQCC OB hemorrhage tool kit

Obstetric Hemorrhage Safety Bundle

Readiness: (every unit)

- Hemorrhage Cart / with Procedural Instructions (balloons, compression stiches)
- Rapid access to hemorrhage medications (kit or equivalent)
- Establish a response team: multiple partnerships, unit education, drills, debriefs
- Establish MTP and o-neg/uncrossmatched transfusion protocols

Recognition: (every patient)

- Assessment of hemorrhage risk (prenatal, on admission, ongoing in labor & PP)
- Measurement of CUMMULATIVE blood loss
- Active Management of 3rd Stage (oxytocin after birth)

Response: (every hemorrhage)

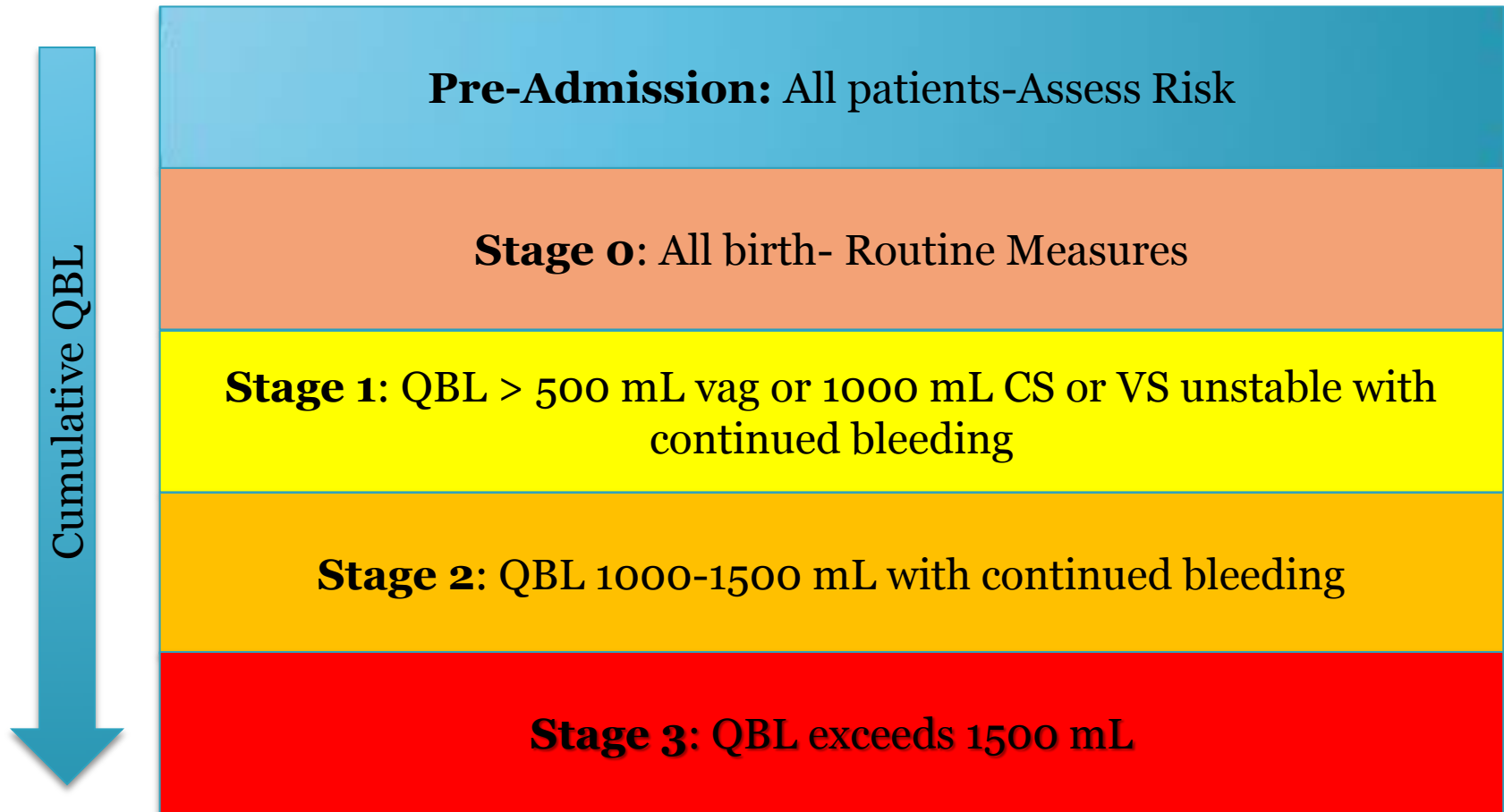
- Unit-standard, stage-based OB Hemorrhage Emergency Management Plan w/checklist
- Support program for patients, families and staff

Reporting / Systems Learning: (every unit)

- Establish a culture of Huddles for high-risk patients and post-event debriefings
- Review all stage 3 hemorrhages
- QI committee monitors outcomes

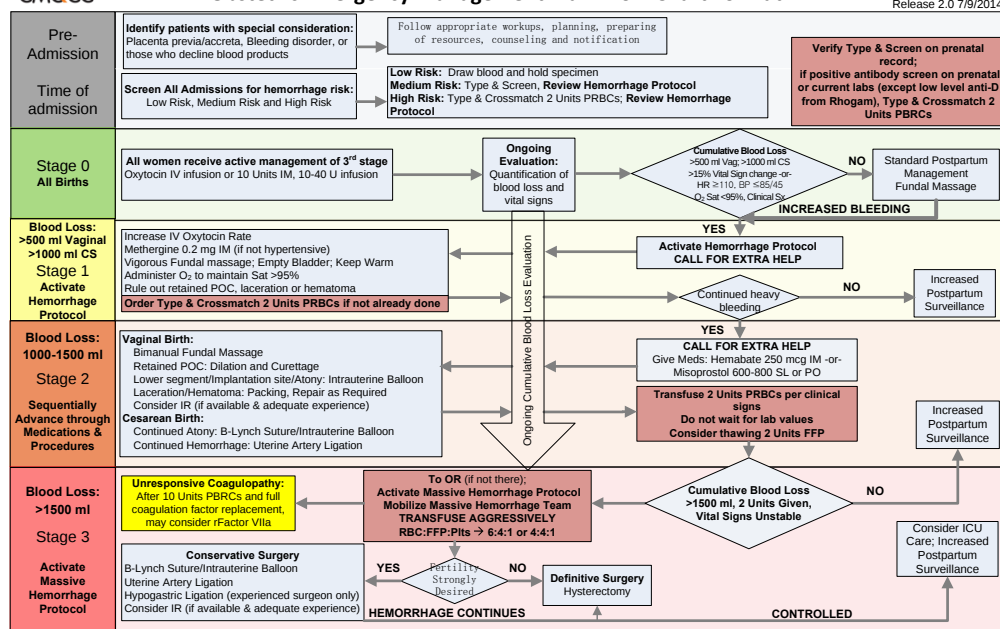


Hemorrhage Guidelines: Staged Responses



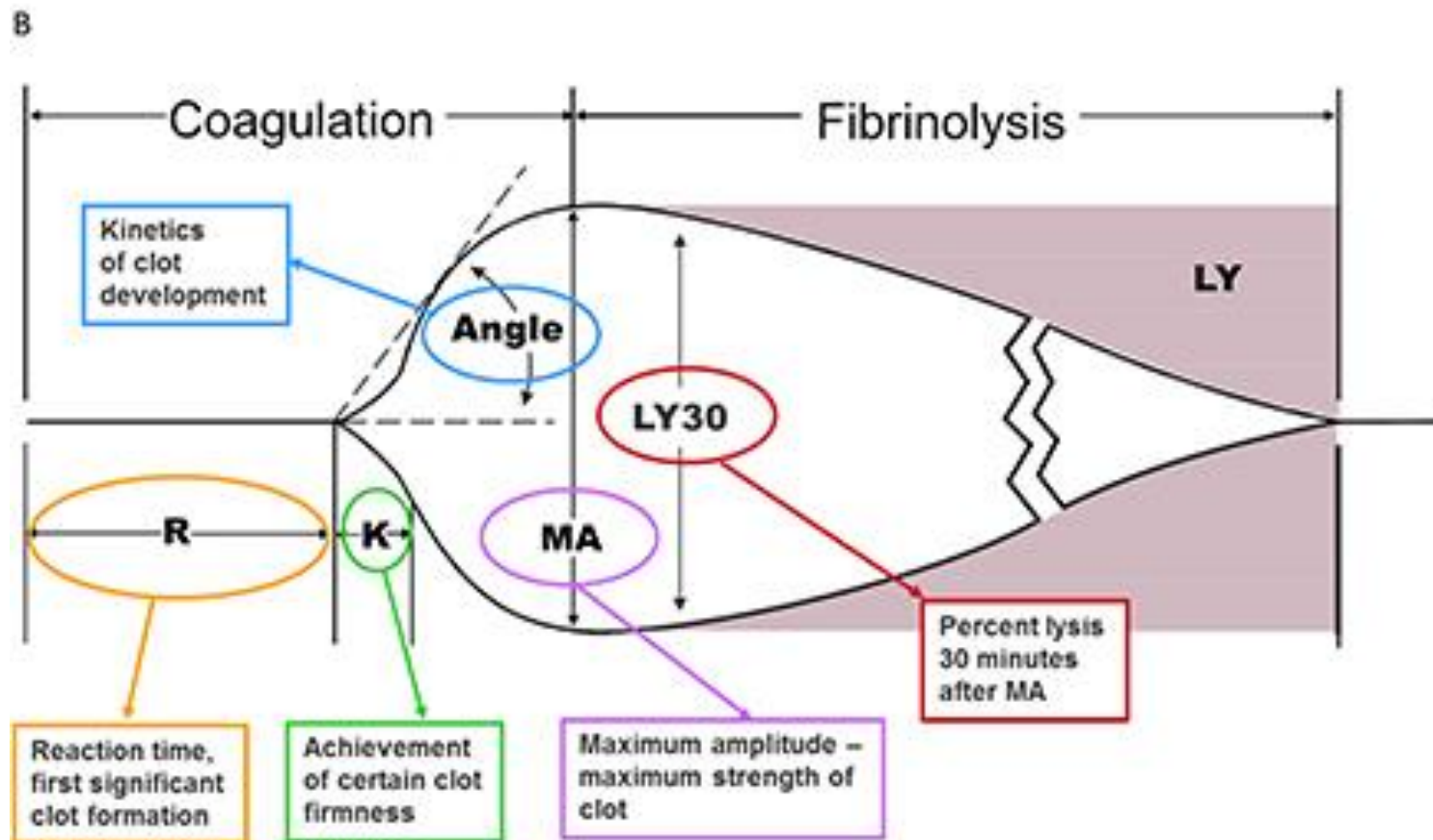
CMQCC OB Hemorrhage Emergency Management Plan

	Assessments	Meds/Procedures	Blood Bank
Stage 0	Every woman in labor/giving birth		
<i>Stage 0 focuses on risk assessment and active management of the third stage.</i>	- Assess every woman for risk factors for hemorrhage - Measure cumulative quantitative blood loss on every birth	Active Management 3rd Stage: - Oxytocin IV infusion or 10u IM Fundal Massage-vigorous, 15 seconds min.	- If Medium Risk: T & Scr - If High Risk: T&C 2 U - If Positive Antibody Screen (prenatal or current, exclude low level anti-D from RhoGam):T&C 2 U
Stage 1	Blood loss: > 500ml vaginal or >1000 ml Cesarean, or VS changes (by >15% or HR ≥ 110, BP ≤85/45, O2 sat <95%)		
<i>Stage 1 is short: activate hemorrhage protocol, initiate preparations and give Methergine IM.</i>	- Activate OB Hemorrhage Protocol and Checklist - Notify Charge nurse, OB/CNM, Anesthesia - VS, O2 Sat q5 - Record cumulative blood loss q5-15 Weigh bloody materials - Careful inspection with good exposure of vaginal walls, cervix, uterine cavity, placenta	IV Access: at least 18gauge - Increase IV fluid (LR) and Oxytocin rate, and repeat fundal massage Methergine 0.2mg IM (if not hypertensive) - May repeat if good response to first dose, BUT otherwise move on to 2nd level uterotonic drug (see below) - Empty bladder: straight cath or place Foley with unmetr	T&C 2 Units PRBCs (if not already done)
Stage 2	Continued bleeding with total blood loss under 1500ml		
<i>Stage 2 is focused on sequentially advancing through medications and procedures, mobilizing help and Blood Bank support, and keeping ahead with volume and blood products.</i>	- OB back to bedside (if not already there) Extra help: 2nd OB, Rapid Response Team (per hospital), assign roles - VS & cumulative blood loss q 5-10 min - Weigh bloody materials Complete evaluation of vaginal wall, cervix, placenta, uterine cavity - Send additional labs, including DIC panel - If in Postpartum: Move to L&D/OR - Evaluate for special cases: - Uterine Inversion - Amn. Fluid Embolism	2nd Level Uterotonic Drugs: Hemabate 250 mcg IM or Misoprostol 800 mcg SL 2nd IV Access (at least 18gauge) - Bimanual massage Vaginal Birth: (typical order) - Move to OR - Repair any tears - D&C: r/o retained placenta - Place intrauterine balloon - Selective Embolization (Interventional Radiology) Cesarean Birth: (still intra-op) (typical order) - Inspect broad lig, posterior uterus and retained placenta - B-Lynch Suture - Place intrauterine balloon	- Notify Blood Bank of OB Hemorrhage - Bring 2 Units PRBCs to bedside, transfuse per clinical signs – do not wait for lab values - Use blood warmer for transfusion - Consider thawing 2 FFP (takes 35+min), use if transfusing > 2u PRBCs - Determine availability of additional RBCs and other Coag products
Stage 3	Total blood loss over 1500ml, or >2 units PRBCs given or VS unstable or suspicion of DIC		
<i>Stage 3 is focused on the Massive Transfusion protocol and invasive surgical approaches for control of bleeding.</i>	Mobilize team - Advanced GYN surgeon 2nd Anesthesia Provider - OR staff - Adult Intensivist Repeat labs including coags and ABG's - Central line - Social Worker/ family support	Activate Massive Hemorrhage Protocol - Laparotomy: - B-Lynch Suture - Uterine Artery Ligation - Hysterectomy - Patient support - Fluid warmer - Upper body warming device - Sequential compression stockings	Transfuse Aggressively Massive Hemorrhage Pack - Near 1:1 PRBC:FFP 1 PLT apheresis pack per 4-6 units PRBCs Unresponsive Coagulopathy: After 8-10 units PRBCs, and full coagulation factor replacement: may consult re rFactor VIIa risk/benefit



Hospitals will need to customize the protocol but the point is every hospital needs one

TEG in OB hemorrhage



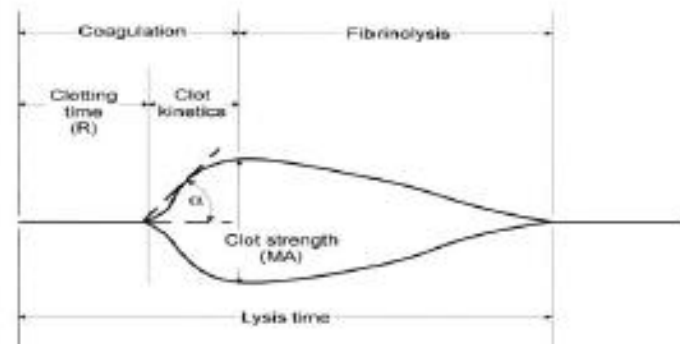
Anderson L, Quasim I, Steven M, et al. Interoperator and Intraoperator Variability of Whole Blood Coagulation Assays: A Comparison of Thromboelastography and Rotational Thromboelastometry. *J Cardiothorac Vasc Anesth.* 2014;28(6):1550-1557.

TEG in OB hemorrhage

Dr. Jonathan Waters SABM 2018 “Point of Care Devices for Guiding Transfusion Decision Making During Postpartum Hemorrhage” – with permission

TEG Clinical Advantages

- Measures entire coagulation cascade in whole blood
- Examines interaction between platelets, clotting factors, and fibrinogen
- PTT, PT, INR, platelets, bleeding time $\Rightarrow$ only measures a **specific** part of the coagulation process (may not accurately predict if a patient is at risk for bleeding)



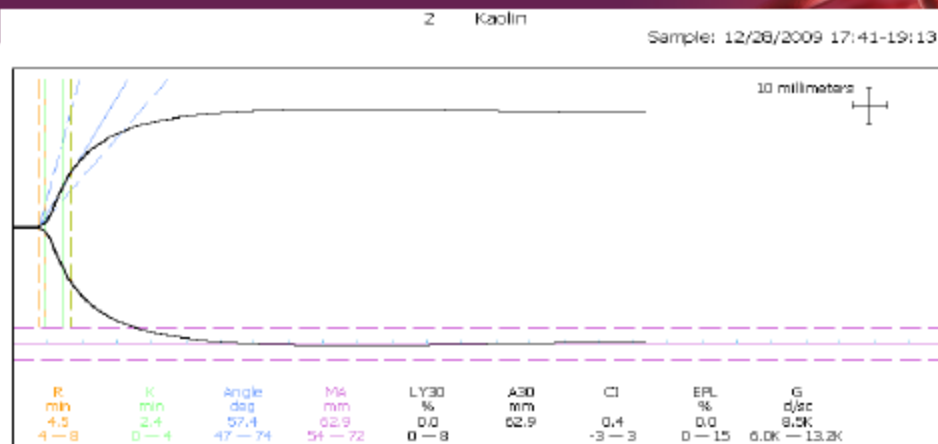
TEG Interpretation

<i>Normal</i>		Normal	Nothing
<i>Anticoagulants/hemophilia</i>		Prolonged R	FFP/Protamine/Humate
<i>Platelet Blockers</i>		Decreased MA	Platelets Cryoprecipitate
<i>Fibrinolysis</i>		Decreased MA 60	Amicar, Tranexamic Acid
<i>Hypercoagulation</i>		Increased MA	Anticoagulation
<i>D.I.G</i>		Decreased R Prolonged R Decreased MA	Platelets FFP, RBC's
<i>Stage 1</i>			
<i>Stage 2</i>			

Case #1

- 21 yr old, gravida 1 @ 34 wks for induction of labor
- Severe pre-eclampsia and HELLP syndrome
- Epigastric pain, BP of 167/103mmHg, thrombocytopenia, elevated AST and ALT
- Laboratory findings: AST 419, ALT 294, ALP 315, uric acid 9.3, **platelet count = 27K**, PT 13.9, PTT 31.2, and INR 1.1

Case #1 TEG



UPMC LIFE CHANGING MEDICINE

- Epidural placed without complications
- SVD 6 hours later
- PP platelet 70K
- Epidural catheter removed without incident

Summary

- Anemia is associated with significant OB and neonatal/pediatric risk
- Transfusion in OB has risk
- Tranexamic acid should be used early in PPH
- Future OB PBM improvements are promising

Patient Blood Management in OB

Pre-
conception

Antepartum

At
delivery

Baby

Postpartum

Patient Blood Management is the timely multidisciplinary application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in effort to improve patient outcome